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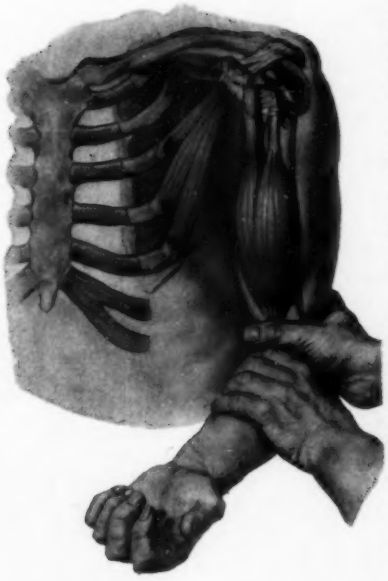

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1. Frankel, C. J., and Strider, D. V.: Presented at Meeting of American Academy of Orthopaedic Surgeons, New York, N. Y., Feb. 3, 1958.

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Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• ISLET CELL TUMOR

Q. For the past 12 years, a 50 year old man has had slurred speech, unsteady gait and weakness occurring at irregular intervals during the day. These symptoms are relieved by the intake of food. On several occasions, urinalysis revealed no sugar. Results of a glucose tolerance test were: fasting blood sugar level 87 mg. per cent, urine sugar none; in one-half hour, blood sugar 99 mg. per cent, no urine specimen; in one hour, blood sugar 91 mg. per cent, urine sugar a trace. At this time the patient began to have the symptoms previously described. At the end of two and one-half hours, blood sugar had decreased to 54 mg. per cent and no urine sugar was present.

Is this functional hyperinsulinism or an islet cell tumor? What do you advise as to diet and further tests before surgical exploration is done?

M.D.—Ontario

A. The history and findings stated are not sufficient to establish a diagnosis of either functional hypoglycemia or islet cell tumor. However, further studies should be done before surgical exploration of the pancreas is seriously considered. Blood sugar determinations should be made at the time the patient is having the symptoms, and further studies should be made of the relief obtained from sugar administered either orally or intravenously.

The response of the blood sugar to a prolonged fast of 48 hours or more is usually of more diagnostic aid than are the results of a glucose tolerance test. During the fast the patient should not be confined to bed, since activity helps to precipitate significant hypoglycemia in persons with functioning islet cell tumors. The blood sugar should be determined when symptoms suggesting hypoglycemia occur, or before the fast is ended, if no symptoms occur. If a functioning islet cell tumor is present, a prolonged fast will cause the blood sugar to drop below 40 mg. per 100 ml. when determinations are made by the Folin and Wu method.

• CLIMATE AND RHEUMATOID ARTHRITIS

Q. Climatic factors have been mentioned repeatedly in connection with rheumatoid arthritis. Do statistics show that some areas of the North American continent are more healthful than others for arthritic patients?

M.D.—New Brunswick

A. There are no convincing statistical studies which indicate the merits of one climate over another for persons with rheumatoid arthritis. Many arthritic patients feel better in the warm, dry climate of the southwestern United States, but it is difficult to separate the effects of climate alone from those of the extra rest and relaxation associated with short stays in such areas. It is agreed that "climate is no substitute for experienced medical supervision." However, some patients can care for themselves more easily in warm, dry areas, and a few appear to have a remission of their active disease. Before making a permanent move, a patient should try living in the new location for at least three months, duplicating the circumstances of his more permanent living conditions.

(Continued on page A-22)

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patients

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the pressures
ON your
patients

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Corrin, K. M.: Am. Pract. & Dig. Treatment 8:721 (May) 1957.

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• RADIOACTIVE IODINE

Q. I have read that the use of radioactive iodine in the treatment of thyroid disease potentiates the danger of future cancer. Would doing a test for thyroid function with this substance present the same danger?

M.D.—Puerto Rico

A. There is increasing evidence that any type of radiation is potentially dangerous from the standpoint of possible induction of leukemia. In using radioactive iodine, it should be borne in mind that the bone marrow does not receive as much radiation following an ordinary therapeutic dose given for hyperthyroidism as it does following an ordinary gastrointestinal series of x-rays. The risk, therefore, is relative. Certainly to date there is no evidence that cancer of the thyroid itself is caused by the use of radioactive iodine therapeutically. There is also very strong evidence in experimental animals that keeping the animal in normal thyroid balance will protect it from any tendency toward the development of cancer of the thyroid after administration of very large doses of radioactive iodine. In effect, this is accomplished by feeding the animal thyroid so that hypothyroidism does not occur. The stimulus in the development of cancer of the thyroid appears to be not so much the radiation itself as it is the secondary effects induced by the suppression of thyroid function and the increase in the amount of thyroid-stimulating hormone secreted by the pituitary. If care is taken to keep the patient in normal thyroid balance, these changes do not occur. Certainly there would be no significant danger in the employment of tracer doses of radioactive iodine.

Second consultant: The potential hazard of carcinogenesis involved in the therapeutic use of radioactive iodine remains theoretical, and has yet to be completely assessed, as there has been no documented instance of cancer attributable to this source during the 10 or 12 years that large numbers of patients have been treated with radioactive iodine.

Since the quantity of radioiodine required for evaluation of thyroid function as a diagnostic procedure is almost infinitesimally small, compared with that employed in therapy, the risk of inducing malignant change with this agent also should prove infinitesimal. Most physicians concerned with the treatment of thyroid disease do not feel that there is any forbidding risk in the use of radioiodine diagnostically. Most of them would, however, urge that restraint be used in application of the procedure among small children, and that, at the very least, radioiodine studies in children be done with an absolute minimum of irradiation, if done at all.

• THIRD HEART SOUND

Q. Could an accentuated third heart sound be considered comparable to the opening snap of the mitral valve in mitral stenosis?

Does a right-sided or left-sided heart-failure always imply eventual heart enlargement? If so, how long does it take for such enlargement to develop?

M.D.—Iowa

A. The third heart sound is very seldom heard with a stethoscope. It is never loud enough to be confused with the opening snap of the mitral valve in mitral stenosis.

Right-sided or left-sided heart-failure is always accompanied by right-sided or left-sided cardiac enlargement, or both. The length of time in which such enlargement develops varies with each case.

Second consultant: The opening snap of the mitral valve *is* a third heart sound, occurring early in diastole in mitral stenosis. So far as is known, the exact origin of this sound has not been established. Diastolic gallop sounds also are third heart sounds, usually occurring later in diastole than the so-called opening snap of the mitral valve. A rush of blood into a dilated left ventricle is believed to contribute to the origin of the gallop sound. In "summation gallop" the normal atrial sound is believed to occur coincidentally with the gallop sound because of delay in atrioventricular conduction, causing the atrial contraction to occur relatively early in diastole.

So-called right-sided failure may occur in the presence of inflow-tract obstruction, as represented in chronic constrictive pericarditis without major cardiac enlargement. When the pathogenesis of heart-failure places an increased load on the ventricular myocardium, cardiac enlargement is the inevitable attendant of chronic congestive heart-failure. The greatest enlargement is seen to develop in the presence of protracted increases in the load of cardiac work. However, acute dilatation of the heart may occur within a period of minutes, as under the circumstances of asphyxia.

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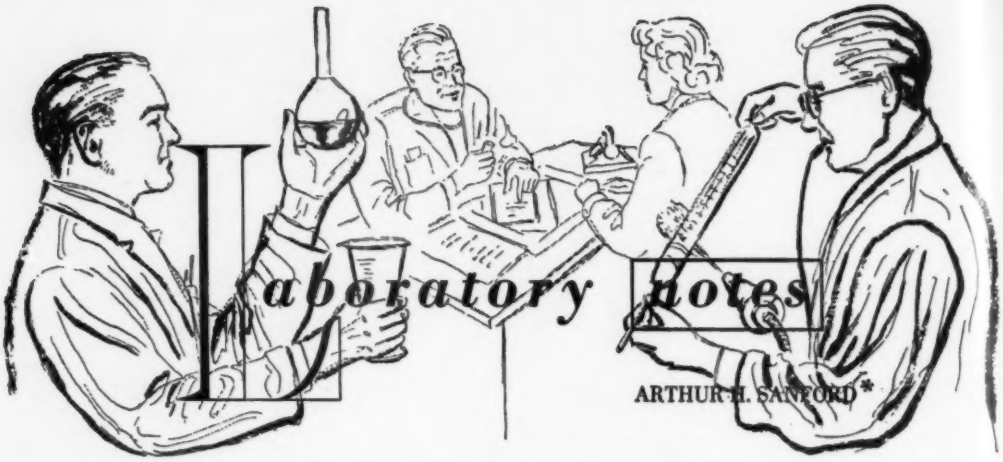


ARTHUR H. SANFORD *

Report: Meeting of College of American Pathologists and American Society of Clinical Pathologists

THE American Society of Clinical Pathologists (generally referred to as A.S.C.P.) was founded in 1922. It has sponsored many worthwhile projects in the field of laboratory medicine, such as initiating and carrying out, with the United States Public Health Service, the evaluation of serodiagnostic tests for syphilis devised in this country. With the Section of Pathology and Physiology of the A.M.A., the A.S.C.P. also sponsored the formation of the American Board of Pathology.

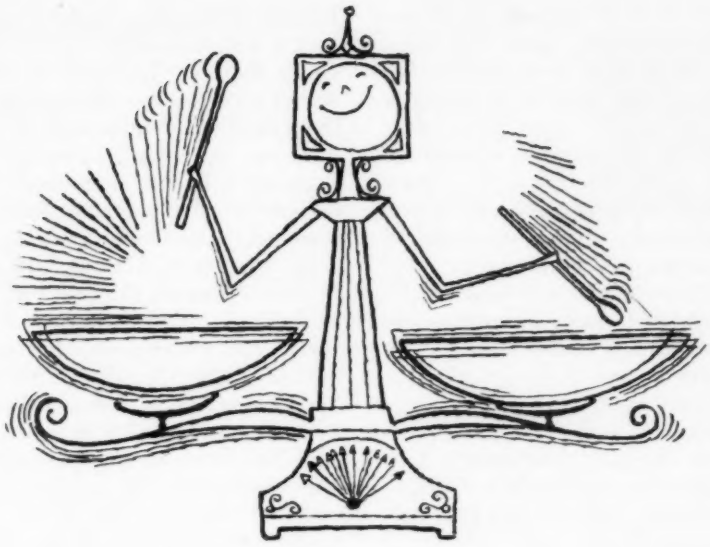
The College of American Pathologists was founded in 1947. Membership in the College is limited to those physicians who have become diplomates of the American Board of Pathology. There is, of course, great overlapping in the membership of both organizations. The meetings, held jointly, follow a certain pattern and last nearly a week, with about 1500 registrations. The committee meetings of the College and the joint scientific sessions of the two bodies usually run through Monday and Tuesday. On Wednesday, the A.S.C.P. starts its independent scientific sessions, completing them on Friday, with a seminar of really hard-working participants. Also running parallel with all these activities are many workshops, held at various hospitals. Some high lights and impressions of the meeting in Chicago in November 1958 may be of interest.

There was a cordial telegram of greetings and best wishes from President Eisenhower.

The Board of Schools of Medical Technology is urging schools to prepare for a new rule, effective in 1962, requiring three years of college plus one year of training in an approved school as a requirement for certification. Currently 452 of the approved schools (66 per cent of the total) are affiliated with colleges, and the training period may be counted toward a degree. The Board of Registry reported that 273,000 pieces of general informational material in medical technology were distributed during the year. Physicians should advise any young acquaintances interested in this field to write to Dr. Lall Montgomery, Ball Memorial Hospital, Muncie, Indiana, for information. Warning must be given against the attractive but grossly misleading advertising in newspapers and magazines of the commercial schools which pretend to train students in medical technology. These commercial schools have very low standards for entrance requirements and only limited facilities for teaching; they also charge tuition entirely out of propor-

(Continued on page A-30)

*Emeritus Staff, Section of Clinical Pathology, Mayo Clinic; Director of Laboratories, Rochester State Hospital, Rochester, Minnesota.



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tion to that of the truly approved schools.

Presented at the meeting were many interesting papers, which will be published. The details of some of these may be discussed in future columns.

Dr. Reuben Straus presented a paper on "Catecholamines: Determination of urinary epinephrine and nonepinephrine levels." There seems to be an increase of these substances in the urine of patients with brain tumors.

Dr. John J. Andujar has developed and reported on an unheated plasma flocculation test for syphilis, which may prove to be a very simple screen test for use in blood banks and the everyday practice of clinical pathology.

The Ward Burdick award, with a gold medal, given by the A.S.C.P., was presented to Dr. T. B. Magath of the Mayo Clinic. The subject of his 30 minute address was "The antigen of *Echinococcus*."

The subject that has attracted a great deal of attention in clinical laboratories during 1958 is "automation." It is suggested that the practice of medicine is two decades behind industry in the matter of developing automatic methods for data handling and in the actual performance of technical procedures. The expense of the apparatus for auto-analysis is excessive; the advantages lie chiefly in accurate results obtained (if all is running right) and in freeing a technologist from doing a large number of tests that may be run daily, such as blood sugar determinations or blood urea nitrogen determinations, so that other less frequently performed tests may be performed at the same time.

The proceeds of the Sheard-Sanford fund that have accumulated from the royalties from the Cenco Sheard-Sanford Photelometer have been used for prizes for some years. Recently awarded prizes were given to students in various medical schools for meritorious research under the direction of the professor of pathology. The list of these prize winners follows:

J. R. Williamson, "Electron microscopy of the islet cells in alloxan-treated rabbits." Pathologist, Dr. Paul E. Lacy, Washington University School of Medicine, St. Louis. Roland Samson, "Investigation on the etiology of chronic Chagas myocarditis." Pathologist, Dr. Rudolph J. Muelling, Jr., Louisiana State University School of Medicine, New Orleans. Melvin D. Reuber, "The effect of adrenalectomy and of cortisone and desoxycorticosterone on the formation of malignant liver tumors in AXC rats ingesting 2-diacetylaminofluorene." Pathologist, Dr. Robert Stowell, University of Kansas School of Medicine, Kansas City. Eric Comstock, "Determination of dopa-oxidase activity in pigmented tissues." Pathologist, Dr. William O. Russell, University of Texas. Stuart Schlossman, "Vascularization of the cornea during delayed hypersensitivity reactions." Pathologist, Dr. Chandler A. Stetson, Jr., New York University College of Medicine, New York. Vernon McFalls, "Genetic study of vitamin D-resistant rickets and hypophosphatemia." Pathologist, Dr. John B. Graham, University of North Carolina School of Medicine, Chapel Hill. William Bullock, "Carrier state in plasma thromboplastin component deficiency." Pathologist, Dr. John B. Graham, University of North Carolina School of Medicine, Chapel Hill. John E. Mielke, "Influence of beta-aminopropionitrile upon development of connective tissue in croton oil pouches." Pathologist, Dr. Murray Angevine, University of Wisconsin Medical School, Madison. Roger Arhelger, "Influence of gram-negative endotoxin on response of rats to nephrotoxic serum." Pathologist, Dr. James R. Dawson, Jr., University of Minnesota Medical School, Minneapolis. Wayne Schrader, "Studies on mechanisms of production of fibrinoid lesions by x-ray and gram-negative endotoxin." Pathologist, Dr. James R. Dawson, Jr., University of Minnesota Medical School, Minneapolis. James M. Anderson, "The influence of acute stress on the response of rabbits to intravenous endotoxin." Pathologist, Dr. James R. Dawson, Jr., University of Minnesota Medical School, Minneapolis. Carl Gunderson, "Origin and potency of the antibody-forming cell of the spleen." Pathologist, Dr. Robert W. Wissler, University of Chicago, the School of Medicine, Chicago. S. Douglas Frasier, "Review of mechanisms of protein biosynthesis and a report on incorporation of lysin N15 into liver proteins of injured rats." Pathologist, Dr. Sidney Madden, University of California.

What's happening in Medicine

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

EYE SURGERY USES LIGHT HEAT

American Academy of Ophthalmology and Otolaryngology:

- A "light coagulation" technic has been used to painlessly destroy malignant and benign lesions in the posterior and anterior eye, heal retinal detachments, seal retinal holes and shrink hemangiomas and aneurysms. A light beam generated by a supervoltage xenon lamp passes through a series of condensing lenses which narrow the beam to a pinpoint. Heat is formed only in dark tissues which absorb light, including the choroid, pigmented epithelium, iris and blood vessels.—Dr. Gerd Meyer-Schwickerath, University of Bonn, West Germany.
- Flicker perimetry has been carried out on a clinical basis using a gray tangent screen and a stroboscopic lamp mounted on a wand. Determinations for selected points in the visual field were made of the maximal frequency of stimulation at which flicker was seen. In diagnosing chronic simple glaucoma, flicker perimetry is often more rapidly performed and less fatiguing to the patient.—Dr. Charles J. Campbell, New York.
- Patients with tinnitus are exposed to noise on the theory that further damage to the cochlea may relieve the ringing by making the nerves less sensitive. Noise is produced by amplifying the sound produced by a beat-frequency oscillator. Average exposure time is 10 minutes. Some patients were relieved for only a few minutes or a few hours, but in some the subjective improvement lasted a month or more.—Dr. George F. Reed, Massachusetts Eye and Ear Infirmary, Boston.

ACTIVITIES OF CARDIAC PATIENTS UPGRADED

American Medical Association Clinical Session:

- Work-classification limitations of heart patients are too low. These patients can safely perform intermittent work that requires much greater energy than that listed in the classification charts. The term "light work" should be removed from the lexicon of cardiac rehabilitation. The emotional impact of work restriction often retards a cardiac patient's rehabilitation.—Dr. Edward E. Gordon, Michael Reese Hospital, Chicago.
- An intragastric-cooling balloon, used to treat massive upper gastrointestinal hemorrhage, enables proper evaluation and preparation of the patient for definitive treatment.—Dr. Owen H. Wangensteen, University of Minnesota Medical School, Minneapolis.
- Twenty-seven patients with pulmonary alveolar proteinosis have been observed in approximately the last three years. Symptoms include labored breathing, cough, chest pain and fatigue. X-ray study shows lung changes that resemble those of severe pulmonary edema. No causative agent has been found.—Armed Forces Institute of Pathology, Washington, D.C.

New horizons in cytology

Inter-Society Cytological Council:

• Cytology has proved its value in studying sterility, pregnancy and threatened abortion, and in diagnosing follicular persistency, amenorrhea and irregular menstrual rhythm. It has been used to study disorders of the menarche and the climacteric and to control the duration and assess the efficiency of hormone therapy. Among its more spectacular possibilities is the detection of pregnancy within a few weeks of fertilization of the ovum.—Dr. George L. Wied, University of Chicago.

• Unsuspected cancer of the colon was detected in 377 patients by microscopic studies of smears of fecal material, mucous scrapings and tissue washed out of the colon in enemas. Some 3000 cytologic examinations were performed.—Dr. R. J. Thabet, Ohio State University, Columbus.

• The urine smear technic can be used as an office procedure to predict with accuracy those women who are inevitable aborters. If adapted clinically, the method will shorten hospitalization and use of hormone therapy.—Dr. Cyril Solomon, French Hospital, New York.

Chorea linked to "strep" infection

American Rheumatism Association:

• For the first time, evidence shows that Sydenham's chorea may follow streptococcal infections, unaccompanied by rheumatic polyarthritis and carditis. Sixty children with a history of Sydenham's chorea, hence susceptible to recurrences, were followed for more than five years. Chorea did not occur among the 41 children who were free from streptococcal infections. However, 3 of 19 children in whom one or more streptococcal infections developed had recurrences of chorea from two and a half to six months after the first evidence of infection.—Dr. Angelo Taranta, Irvington House, Irvington, N.Y.

• The intradermal or intra-articular administration of serotonin to patients with rheumatoid arthritis and related diseases results in an exaggerated reaction, which can be neutralized in vivo by certain serotonin antagonists. The altered response may be a clue to the role played by biochemical abnormalities in nerve activation in rheumatoid arthritic symptoms, such as muscle atrophy, depressive reactions and emotional instability.—Dr. Arthur L. Scherbel, Cleveland Clinic, Cleveland.

Grafting saves limbs

Gerontological Society:

• Grafting procedures are sufficiently established that amputation should not be considered in obstructive arterial disease without evaluating the possibility of re-establishing circulation. Limbs can be saved in about 30 per cent of patients facing amputation.—Dr. Brooke Roberts, University of Pennsylvania Hospital, Philadelphia.

Early resection advised for rectal cancer

American Cancer Society:

• Combined abdominoperineal resection with permanent abdominal colostomy offers the best chance for cure or long-term survival in cancer of the rectum. Disregarding the zone of downward spread is not justified. Even when an adequate abdominoperineal operation has been done, a number of perineal recurrences have occurred, some as long as six years after the operation.—Dr. Calvin M. Smyth, Abington Memorial Hospital, Abington, Pa.

Radiology FOR PRACTICING PHYSICIANS

Giant-cell Tumor of Bone

PAUL C. HODGES*

FORTY years ago leading American teachers of orthopedic surgery, pathology and radiology were convinced that the lesion we now call giant-cell tumor, which at that time was generally known as giant-cell sarcoma, was, in fact, a benign condition. They advised that amputation or other radical surgery for this condition be replaced by much more conservative treatment and that the term "benign giant-cell tumor" be substituted for "giant-cell sarcoma." The teaching was accepted rather promptly, and undoubtedly the change in attitude spared many patients unnecessarily drastic surgery; but with the passage of the years, it has become apparent that against this gain there must be set the loss of some lives that might have been saved. Today it is recognized that all giant-cell tumors are potentially malignant and that although many can be cured by local extirpation and others by extensive surgery even after local recurrence, a few will soon metastasize, killing their hosts.

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Jaffe,[1] whose new book is enormously informative in this as in many other phases of skeletal disease, says that more than half the tumors recur locally after curettage, even when they are not histologically sarcomatous, and that the over-all incidence of metastasis is 15 per cent.

Unfortunately, even when a pathologist is supplied with generous biopsy specimens, uncomplicated by hemorrhage, infection or previous therapy, his principal contribution is to confirm whether or not a particular lesion is a giant-cell tumor and is already frankly sarcomatous. He has criteria for dividing nonsarcomatous giant-cell tumors into either a group likely to recur after curettage or a group unlikely to do so; however, he recognizes that in doing this he makes many errors of commission and omission. Thus, while the combination of clinical, radiologic and histologic evidence establishes the diagnosis of giant-cell tumor with a high degree of accuracy, predictions of the degree of potential malignancy are uncertain; it is best to treat all

FIGURE 1a and b. Frontal view and lateral view of a giant cell tumor at the proximal end of the tibia in a 34 year old man.

FIGURE 2. Giant-cell tumor at the proximal end of the humerus in a 33 year old man.

of the giant-cell tumors with healthy respect.

The current term "giant-cell tumor" reflects this thinking, avoiding both the "benign" of the optimists and the "sarcoma" of the pessimists. Histologically, it denotes an entity characterized not merely by multinuclear giant cells but by characteristic stromatic cells as well. Radiologically, it denotes a relatively uncommon bone-destroying tumor of patients who are rarely much less than 20 or much more than 50 years of age. Almost all giant-cell tumors occur at the ends of the long tubular bones, where they are easy to diagnose and treat. Diagnosis and treatment are more difficult in those uncommon instances of involvement of the spine, skull, ankle bones or other flat or irregular bones.

The following discussion of the x-ray criteria for diagnosing giant-cell tumor, for attempting to determine whether it is malignant and has begun to invade locally, and for differentiating giant-cell tumor from two other conditions is based on the conditions that are illustrated.

Diagnosing Giant-cell Tumor

Figure 1 shows a typical giant-cell tumor in a patient who is well within the usual age range (34). The tumor is bone-destroying and circumscribed and is located at the end of the shaft of a long tubular bone, in this instance the tibia. It shows no evidence of bone production, lies partly in the shaft and partly in the epiphysis, and excavates up close to the articular surface of the bone.

A typical giant-cell tumor in a 33 year old

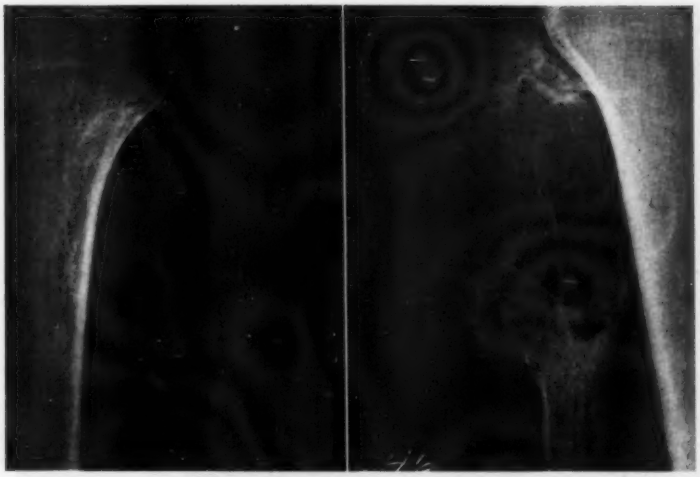

FIGURE 3. Giant-cell tumor at the proximal end of the fibula in a 40 year old woman.

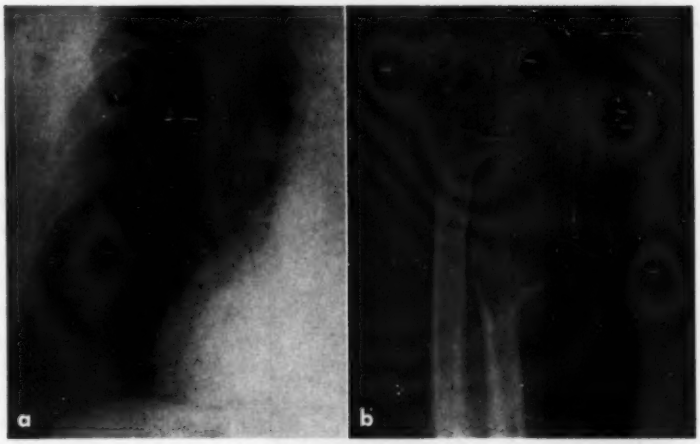

FIGURE 4a. A solitary nodule in the lower third of the left lung in a 59 year old man. This was thought to be metastasis from the benign giant-cell tumor at the distal end of the ulna; at operation, it proved to be benign hamartoma. b. Extensive destruction of the cortex and extension of the tumor into soft tissue, erroneously assumed to indicate that the giant-cell tumor was malignant. It was, in fact, benign; the cortex had been destroyed merely by pressure necrosis.

man is shown in figure 2. As in the case illustrated in figure 1, the lesion destroys bone and does not produce it. It lies at the proximal end of the shaft of the humerus, extends into the epiphysis, and excavates up to the articular surface. In neither of these two cases is there much evidence of the trabecular pattern, which has been so stressed in some of the earlier radiologic writing. It is true that trabeculation sometimes is seen, but it is so often absent that its presence has become an argument against rather than in favor of a diagnosis of giant-cell tumor.

That trabeculation does sometimes occur is illustrated in figure 3. This is a proved giant-cell tumor in the proximal end of the shaft of the fibula in a 40 year old woman. It has produced gross fusiform expansion of the upper portion of the fibular shaft and has extended into the proximal epiphysis; it appears to have broken through the cortex distally and shows a rather marked degree of trabeculation. Microscopic examination following resection showed that it was, in fact, a giant-cell tumor with no evidence of malignancy. It had broken through the cortex simply by virtue of its size. In keeping with the older teaching and in contradiction to present-day experience, there is

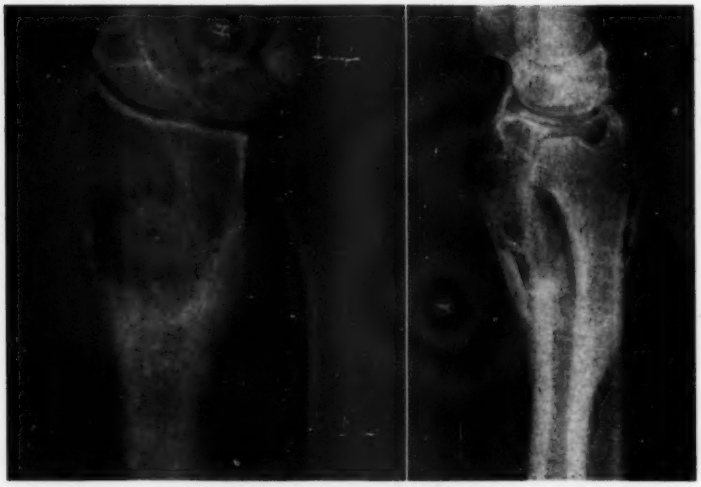

FIGURE 5. Typical giant-cell tumor at the distal end of the shaft of the radius in a 25 year old woman.

FIGURE 6. Giant-cell tumor at the distal end of the humerus in a 25 year old woman. This tumor recurred twice following local surgery, but finally responded to resection of the distal end of the humerus.

trabeculation in the grossly thinned and expanded cortical shell.

It has not been sufficiently emphasized that giant-cell tumors do not need to be malignant in order to break through the cortex and to spread into adjacent soft tissue; they may do so through pressure necrosis in a manner analogous to the perforation of the sternum by a large aneurysm of the thoracic aorta. The case illustrated in figure 4 is atypical in many regards. The patient is 59 years old and, therefore, beyond the usual upper age limit. This tumor at the distal end of the ulna is so large and so apparently invasive that if it is a giant-cell tumor at all it appears to be one that is highly malignant. The assumption of malignancy seems to be borne out by the presence of a solitary metastasis in the lower third of the left lung. On exploration, however, the lung lesion proved to be a benign hamartoma, and the lesion in the ulna was found to be an enormous but benign giant-cell tumor which had been allowed to grow so large that it had destroyed the cortex by pressure necrosis and then pushed on out into adjacent soft tissue.

To offset the unusual features of the case illustrated in figure 4, figure 5 shows a giant-cell tumor that is obeying all the rules of the game. It is located at the distal end of the radius in a 25 year old woman. It has expanded the shaft, has crossed the epiphysial line,

FIGURE 7a. Lesion at the distal end of the humerus in a 52 year old woman. Although the lesion simulated giant-cell tumor, it actually was caused by parathyroid disease. b. Two and one-half years following surgical removal of a parathyroid adenoma.

FIGURE 8. Chondroblastoma at the head of the femur in a 16 year old girl. This type of lesion is sometimes mistaken for giant-cell tumor.

and has excavated right up to the articular surface. It shows no evidence of invasiveness and is not trabeculated.

Figure 6 shows another giant-cell tumor typical in many respects and with no radiologic evidence of malignancy. At the age of 24 this young woman began to have pain and limitation of motion in her left elbow; this film was made approximately one year after the onset of symptoms. We diagnosed a giant-cell tumor which was well circumscribed, which destroyed rather than produced bone, and which excavated across the epiphysial line right down to the articular surface at the elbow. Because of our respect for the malignant potentialities of all giant-cell tumors, our surgeons advised resection of the elbow joint, but this was declined by the patient. In an effort to save the joint, the tumor was excised locally and the defect filled with bone chips; except for limitation of extension, the patient did well for a year. Then there developed clinical and x-ray evidence of local recurrence, which failed to respond to further localized surgery and irradiation. The distal end of the humerus was resected approximately three years after the onset of symptoms, and three years later there had been no further recurrence.

Confusion of Giant-cell Tumor With Other Conditions

The older literature is badly confused with publications of the period when giant-cell tumor as we know it today was being separated as an entity. But one must remember that even now and perhaps for all time one will observe localized osteolytic metastases, fibrosarcomas, solitary myelomas, atypical chondrosarcomas and other lesions which on radiologic grounds alone cannot be differentiated from giant-cell tumors. There are, however, other diagnostic errors which can be avoided.

Figure 7a illustrates a localized osteolytic lesion at the lower end of the humerus in a 52 year old woman. Superficially, it looks very much like the giant-cell tumor illustrated in figure 4. It destroys bone rather than producing it; it occurs at the end of a long tubular bone, crosses the epiphysial line, and excavates right down to the articular surface. The fact that the patient is 52 years old argues somewhat against the diagnosis of giant-cell tumor, but in figure 5 we saw a genuine giant-cell tumor in a 59 year old patient. Note, however, that in addition to localized destruction, this patient has a regional osteoporosis, which

should not be present in giant-cell tumor. On investigation the osteoporosis was found to be generalized; additional localized lesions were found elsewhere in the skeleton, and a diagnosis of parathyroid disease was made. In the absence of local surgery, both the generalized osteoporosis and the localized destruction improved following the surgical removal of a parathyroid adenoma (figure 7b).

Figure 8 illustrates a benign chondroblastoma in the head of the femur of a 16 year old girl. We did not mistakenly diagnose it as a giant-cell tumor, but that mistake is sometimes made and presumably explains most, if not all, the reported instances of giant-cell tumor in subjects less than 20 years of age. Like giant-cell tumor, this chondroblastoma crosses from the neck into the epiphysis and excavates down to the articular surface; however, even aside from the age of the patient, the multilocularity of the lesion argues against giant-cell tumor.

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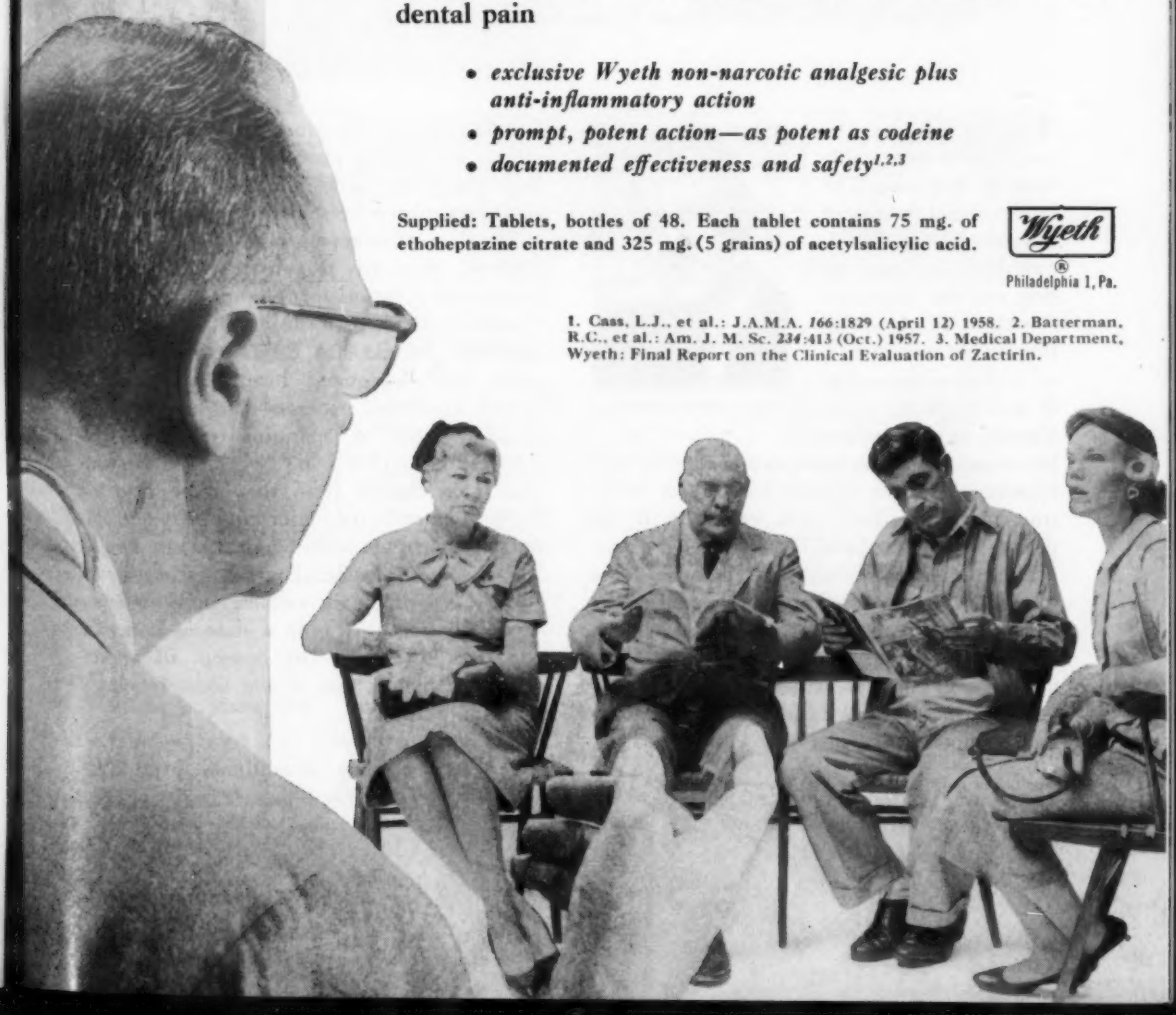

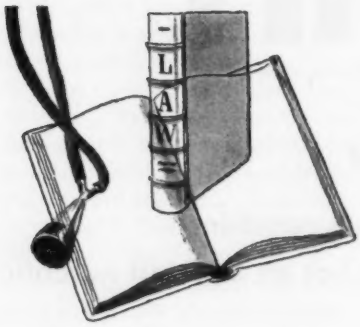

Forensic Medicine

Trauma and Neurosis

HERBERT C. MODLIN

The Menninger Foundation, Topeka, Kansas

HERBERT C. MODLIN

TRAUMATIC neurosis used to be a respectable medical diagnosis. The latest official listings of illnesses by the American Medical Association and the American Psychiatric Association do not recognize it as a diagnostic entity. It still appears occasionally in the medical literature and seems firmly entrenched in legal terminology. A description of the two terms, trauma and neurosis, will explain why the phrase is denied official medical recognition.

Neurosis, or psychoneurosis, is much easier to discuss than to define. It is usually compared for semantic purposes with psychosis. Neurosis, a minor psychologic illness, does not severely disrupt personality functioning but nevertheless may be incapacitating. Common symptoms are anxiety, with its accompanying somatic functional disturbances; specific incapacitating phobias (for closed spaces, high places, etc.); obsessive, ruminative thinking; compulsive acts and rituals; hysterical conversion phenomena, and depression. By contrast, psychosis is a major disruption of personality functioning and corresponds roughly to the legal term insanity. The classic psychotic patient has fixed, irrational delusions, faulty judgment, bizarre symbolic behavior, emotional excesses and, in general, a variable degree of separation from reality as the rest of us know it. Neurosis may vary greatly in degree from the minor neurotic traits common to the majority of people to sets of symptoms clinically definable as illness. Neurosis is the external manifestation of unconscious psychologic conflict, and is evidence that the personality is in a state of upheaval and disequilibrium. The concept of unconscious conflict is one of the basic tenets of dynamic psychiatry.

Dynamic psychiatry is a term peculiar to American medicine. Traditional psychiatry,

(Continued on page A-52)

Parts of this paper have been published previously (NACCA Law J 10:205-215, 1952; J. Kansas Bar A. 14:341-351, 1956).

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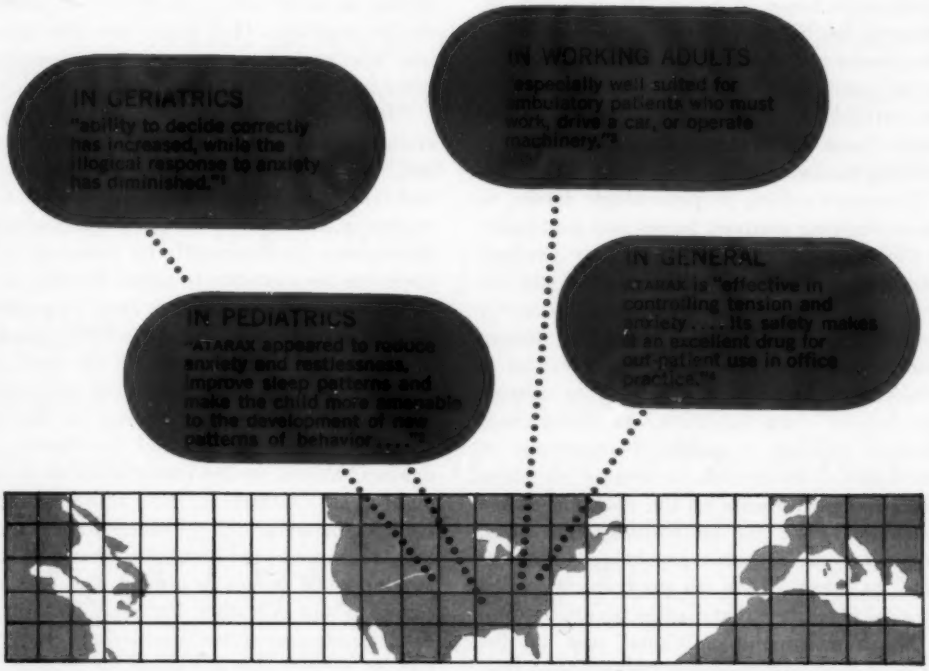
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by contrast, is called descriptive psychiatry. The descriptive psychiatrist endeavors to apply scientific knowledge and skill to the difficult task of identifying and classifying abnormal human behavior. He observes the patient, describes the symptoms and behavior, and arrives at a descriptive diagnosis. The dynamic psychiatrist hopes to do all this, too; but, influenced by Sigmund Freud's epoch-making discoveries and the steadily advancing authority of psychoanalytic theory and technic, he is not satisfied with clinical description as the entire basis for making diagnoses and prescribing treatments.

Dynamics refers, in psychologic terms, to the underlying motives, forces and particularly the purposes of an illness. Many persons, among them many of my colleagues, still believe that, as Dr. Karl Menninger[1] so nicely puts it, "the world is full of healthy human beings, and that now and then a victim is struck down by a cruel blow from an unheeding Nature" (an infection, an unfortunate physical accident, a sudden bereavement or privation). "As a result, a 'disease' develops and a patient appears on the doorstep of the physician."[1] We are increasingly convinced, particularly as concerns psychologic illnesses (and to some extent as concerns so-called physical illnesses), that disease occurs because of forces within the individual, and not because of some unforeseeable perversity of fate. In the inner (psychologic) world of man, there are still large areas of mystery, but all the evidence we have been able to gather indicates that each individual has an innate potentiality for many kinds of behavior including aggressiveness, self-destructiveness, and getting sick.

Dynamic psychiatry rests on several principles, the most important of which is the concept of the unconscious mind, hypothesizing a conscious layer of the mind in contact with reality and capable of judging, thinking, learning and controlling, and adapting the behavior of the human organism of which it is a part. There is also an unconscious layer of the mind, inaccessible to both the possessor and the untrained observer. In this unconscious stratum repose repressed and forgotten memories, painful experiences, unacceptable desires, antisocial strivings and powerful emotions.

Through modern dynamic psychiatry we learn that the ideas and emotions of the unconscious mind are held in check—repressed—and do not usually come to the conscious layer of mental activity. Nevertheless, the unconscious, in subtle ways, influences the behavior of the organism. One might ask why it matters whether conscious or unconscious processes motivate the individual.

"It is because the processes of which we are conscious can be influenced by appeals to reason, by argument and exhortation, by success and failure, by rewards and punishments. Consequently, that part of the personality which is determined predominantly by conscious processes has the capacity to adapt flexibly to external realities and to learn from experience. To the extent, therefore, to which conscious processes govern our lives we are free, free to learn and to grow in wisdom and understanding. Such freedom indeed is the only psychological freedom which psychiatry recognizes; and it is the essential core of normality. In contrast to this, those thoughts, feelings, behavior and personality traits which are determined predominantly by unconscious psychological processes are for that very reason rigid and inflexible. Precisely because the determining forces are unconscious they cannot be swayed by argument or reason, by exhortation or persuasion, by appeals to feelings or to loyalty, by rewards or punishments. Consequently, to the extent to which behavior is driven by unconscious forces it can learn nothing from experience and can never develop or change or grow. In the truest sense of the word, it is enslaved.

"That is why the relative role of conscious and unconscious psychological processes in human affairs is perhaps the most important single fact that can be determined about human personality, human behavior, and human institutions.

"Neither conscious nor unconscious processes ever operate separately. A mixture is always at work; and the distinction between normality and neurosis is relative rather than

(Continued on page A-54)

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absolute. The more predominant the influence of conscious forces, the more normal the behavior; the more predominant the unconscious drives, conflicts and emotions, the more neurotic the behavior."[2]

To illustrate this concept I might cite the behavior of one of my patients. She is invariably late for her 2:00 P.M. appointments. Occasionally she is only five minutes late, but often 30 minutes. I dismiss her promptly at 2:50 P.M., no matter when she comes, and I charge her the full hour's fee. She is the loser in time and money and she knows it. She is distressed by her behavior, but she cannot control it. Descriptively this behavior can be categorized as a simple habit; dynamically it serves irrational (unconscious) purposes, some of which I have discovered. First, she is afraid of me. We really have a good relationship. She needs and sincerely wants my help. She knows that I am devoting myself to her treatment, yet she is unaccountably afraid. She was surprised to learn of her fear; it has become evident that she fears all male adults. Second, she strives constantly for independence; she fears any dependent relationship. Therefore, she struggles against putting herself in my hands. She has to break my "rule." She has to come at her own pleasure, as she dictates, and not as I ask, in order that she may preserve an illusion of self-sufficiency. There are other meanings also, and they are of deeper unconscious significance.

Neurotic symptoms which are uncomfortable and handicapping are evidence that irrational, unconscious mental conflict is producing psychologic upheaval. Development of an incapacitating neurotic reaction depends on two factors: a personality weakness or predisposition to break down, and some stressful situation in the environment to which the patient reacts by getting sick. Some people do not grow and mature so successfully as others, and these immature, psychologically defective persons are prone to adjust abnormally to difficult life situations. Most of them are psychologically weak, or inadequate in only certain unhealthy areas of functioning, largely determined by specific experiences during childhood and adolescence. A girl reared in Victorian prudery may have great difficulty adjusting to the sexual aspect of marriage. I saw such a patient recently; she became so ill on her honeymoon that she had to be hospitalized. A boy reared by a harsh, punitive, restrictive father may have trouble with bosses and supervisors the rest of his life. Both these persons may function well in many areas of human endeavor but be susceptible to stress in specific areas suggestive of their past difficulties and conflicts.

The predisposition for the development of a neurotic reaction is often hidden or masked. As Smith and Solomon[3] have written, "A plaintiff can always bring trusting neighbors to court bearing witness to his hale and hearty pre-accident health and ready to describe calamitous changes noticed in him shortly after receipt of the impact."[3] From the commonsense view these observations are honest, but the pretraumatic condition of the neurotic may not be noticed by the unobservant or untrained eye. In World War II much was learned about the relationship between precipitating stress and predisposition to neurosis. Some men became neurotic before arriving at the induction station; another group broke down during basic training; still others collapsed in advanced training when subjected to live ammunition for the first time; and still others experienced heavy combat before neurosis developed.

This brief discussion of predisposition or susceptibility to stress leads to the second word of our topic, trauma. Trauma means injury from external sources, and the phrase traumatic neurosis indicates that a neurosis has been precipitated by accidental or traumatic means. Neurotic illness in many persons develops gradually over weeks or months, and the stress to which these persons are reacting may be long-standing, as exemplified by an unsatisfactory marital relationship, increasing pressure of work, or a chronic physical illness. Some neuroses seem to be precipitated by a single severely stressful experience such as an overwhelming fright, the unexpected death of a relative, or sudden rejection of a fiancé.

The so-called traumatic neurosis is pre-

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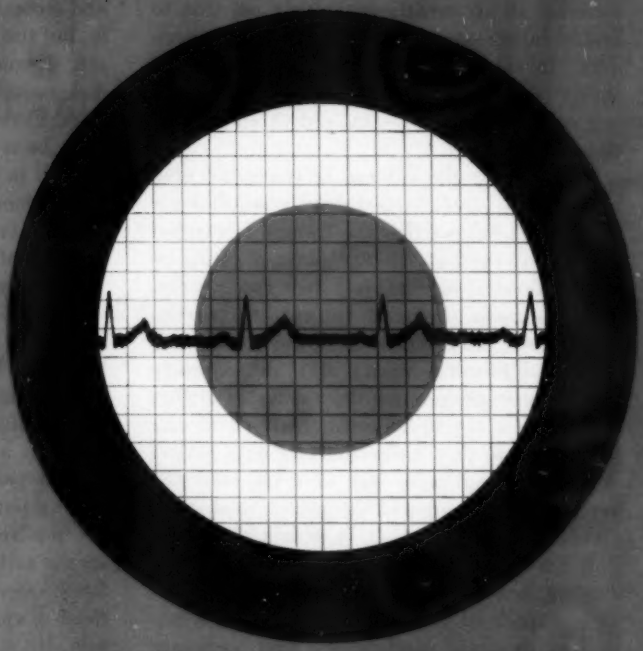

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sumably an abnormal psychologic reaction to bodily injury or severe fright caused by accident. In the majority of cases the physical injury is minor or nonexistent and the resulting nervous reaction seems out of all proportion to the injury.

Just what is the trauma in traumatic neurosis? Since neurosis is a strictly psychologic reaction, it follows that the trauma is psychologic. With the possible exception of brain injuries, physical injury itself does not, *cannot*, cause neurosis. Physical injury and psychologic strain may result from the same accident, and physical injury may subsequently produce unconscious neurotic conflict. Patients may have a severe neurotic reaction to the loss of a limb or a disfigured face or a period of excruciating pain, but in each case the psychologic meaning of the injury to that individual is what lights up a neurotic process.

When the physical injury is trivial or nonexistent, how may we understand the psychologic impact of the accident? There are numerous dynamic mechanisms that variously apply to different cases, but the common denominator is unusual fear. Most of us are fearful in a variety of circumstances without suffering subsequent neurotic incapacity, but in predisposed individuals certain types of fear-producing situations prove to be temporarily overwhelming.

When faced with seemingly dangerous situations, the two common mechanisms most of us use are anticipation and action. If one is aware of potential danger one can frequently anticipate it, prepare to meet it psychologically and emotionally, and withstand the impact when it comes. In so many of the traumatic neuroses I have seen, surprise was a significant element. This is particularly true if the accident occurs in secure, familiar surroundings. In presumably safe circumstances one's psychologic guard is down and one is more vulnerable.

In one case a railroad employee was carrying out a routine job he had done for many years, cleaning a boiler. He released the pressure and removed the manhole cover, only to be unexpectedly knocked off the ladder by a cloud of escaping steam. He had first-degree and second-degree burns which healed promptly, but the rapid development of tension, anxiety, stomach trouble, insomnia, nightmares and irritability kept him from returning to work. Now, a year and a half after the accident, he is still incapacitated and cannot bring himself to get near a boiler.

A second, biologically basic mechanism the human (or even nonhuman) organism uses in the face of fancied or actual danger is action. The fundamental possibility is either to run away or to attack, and we call this instinct for action the fight-flight mechanism. The best antidote for fear is to do something about it. In certain circumstances danger is seen but action is blocked, and the anxiety and tension build up without possibility of discharge.

Two years ago a man who ultimately became a patient and a plaintiff was driving his car in a Nebraska town at dusk. The car stalled on the railroad tracks. As the man waited for the flooded engine to drain, he suddenly noticed a switch engine moving slowly toward him. He stared in fascinated horror as it bore down on him and hit his vehicle. No action was possible, either to start the car or to get out and run. He had 10 to 15 seconds to anticipate annihilation, and the results were catastrophic. Physically his injuries consisted only of some bruised ribs. Psychologically he was a wreck when I saw him eight months after the accident.

The element of surprise and the inability to take action are two elements in many sudden accidents. The person deprived of opportunity to prepare himself or to escape usually will feel a more overwhelming sense of catastrophe. There are other mechanisms operating to increase the emotional intensity of accidental experiences, but these two illustrate the possibilities and partially answer the question of what the trauma is in traumatic neurosis.

In medical and in legal literature on traumatic neurosis another term, compensation neurosis, appears regularly. The connotation of this term is derogatory to the patient to whom it is applied. At times it is used almost as an epithet with the implication of money-grabbing. Of course as a diagnostic term it is

(Continued on page A-58)

have you seen a patient with

*Vogt-Koyanagi syndrome?**

then you should know...

It has been reported[1,2] that patients with the Vogt-Koyanagi syndrome benefit from METICORTEN. Extensive literature indicates that practically every corticosteroid-responsive disorder may be expected to benefit from this established steroid.

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2. Soss, T. L.: California Med. 87:266, 1957.

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In bronchial asthma, poli... Meticorten, New York, ... Letter 27:324 (May 21) ... Dis. Chest 27:515, 1955. ... Studies of metacortandrac... ternat. Conf. Meticorten, ... Prensa med. Venezolana ... Corona, L.: Meticorten e... quimico (Meticorten in t... cal study), Presented a... Janeiro, November 1955. ... osteoarthrosis), First Pan... (16) Bianchi, W., and ... rheumatoid arthritis, Fir... gust 14-19, 1955. (17) Bl... erman, H. A.; Beck, G. ... R. L.; Bollet, A. J.; Sega... tion of metacortandracin... Atlantic City, June 3-4, ... J. J.: Observations on p... thritis, First Internat. ... (21) Blais, J. A.; Duss... M.; Long, L., and Vail... diseases, Ann. Meet., ... (22) Boland, E. W.: Prel... arthritis, Ann. Meet., A... E. W.: Preliminary clini... First Internat. Conf. M... E. W.: California Med. ... ment of lupus erythemat... June 1, 1955. (26) Bollet... 11) 1955. (27) Bollet, A... erythematosus with meta... Assoc., Atlantic City, Ju... and Tedeschi, G. F.: Mi... and Ficini, M.: Minerva... ences with metacortandra... Rheumat., Rio de Janeir... Comparative studies of ... Conf. Meticorten, New ... Acad. Med. New Jersey ... Costa, P.: O Hospital ... (Nov. 13) 1954. (35) Bu... Soc., Philadelphia, May ... 1955. (36) Bunim, J. J. ... York Acad. Sc. 61:358, ... Preliminary observations ... properties of metacortan... Assoc., Bethesda, Maryl... Bollet, A. J.: J.A.M.A. ... and Bollet, A. J.: Ann. ... and Bauer, W.: A compa... nitrogen, and carbohydra... June 3-4, 1955. (41) ... (42) Carrizosa Argaez, ... posium, National Librar... C. A.; Orcese, L.; Zana... (44) Cecil, R. L., in: C... Philadelphia, W. B. S... Wallace, E. Z., and Jail... secretion in the human... June 1, 1955. (46) Cog... arthritis, First Interna... (47) Cohen, A.; Turner, ... with metacortandracin ... New York, May 31 and ... others: Rev. rhum. 22 ... (49) Craver, L. F.: N... Virginia M. Month. 82 ... metacortandracin in var... May 31 and June 1, 19... experiences with Metico... June 1, 1955. (53) De... Ragan, C.: J.A.M.A. ... 8:545, 1955. (55) Dordi... at New York Rheumat. ... E. J.: Studies on the ant... Internat. Conf. Meticort... and Gluck, E. J.: J.A.... E. J.: A.M.A. Arch. ... and Baquiche, M.: Sch... and comments: J.A.M.A. ... 1955. (62) Farah, L.; G... Occid. 1:243, 1955. (63) ... 1955. (64) Ferencz, C.: ... of metacortandracin in ... Meticorten, New York, ... Mosca, M. C., and Ter... V.; Ginoulhiac, E.; ... (July 4) 1955. (67) F... and Carbone, J.: The ... measured by pituitary ... secretion in man, First ... (68) Freisleder, Von ... R. H.: Experiences wit... dralone for in-patients ... York, May 31 and June ... (July 4) 1955. (71) Ga... the treatment of rheun... Rheumat., Rio de Jane... Meticorten in lymphom... York, May 31 and Ju... (74) Gluck, E. J.; Bra... (Sept. 22) 1955. (75) ... 25:75, 1955. (76) Gottl... Merrick, E. P.: J. Am. ... Zabaleta, I., and Palac... (Clinical experiences wi... Rio de Janeiro and Sao... 54:262, 1955. (80) Har... disorders: The effect of ... corten, New York, May ... et al.: Treatment of s...

medically unacceptable, although the basic idea is not completely invalid. Psychiatrists prefer the term secondary gain. It seems to us a more accurate explanation because it is applicable to all neurotic states. Most patients in whom neurotic reactions develop on the primary basis of an unconscious psychologic conflict discover inevitably that there is a certain perverted value in illness and commonly they are prone to exploit it. They may find themselves recipients of all sorts of attention, sympathy and gratification not easily available to a person in good health. They may discover that they prefer special diets, need to eat at odd times of the day or night, require special sleeping arrangements, cannot be left alone, are unable to entertain themselves, must spend long hours in bed, or are unable to pursue gainful employment.

A patient I saw recently has been neurotically incapacitated intermittently for several years. Because of a sensitive stomach she thinks she needs a special diet which her doting mother is happy to prepare. Because of her headaches the TV has to be turned off at times. To cheer her depressed mood numerous persons telephone and drop in to visit her. Because of fatigability she is unable to help with the housework although in the evening she often enters spiritedly into a game of cards. Through her legitimate neurotic illness this patient controls and dominates her family, fashions her own environment, and in some ways "never had it so good." It goes without saying that in many ways she is very much the loser. This is secondary gain. The primary gain of the illness is that the outbreak of symptoms, although painful and incapacitating, helps maintain psychologic equilibrium during stress. The secondary gain comes later as the patient finds some compensations in his disabled state. Both primary gain and secondary gain are unconsciously determined, but secondary gain may have elements of conscious motivation.

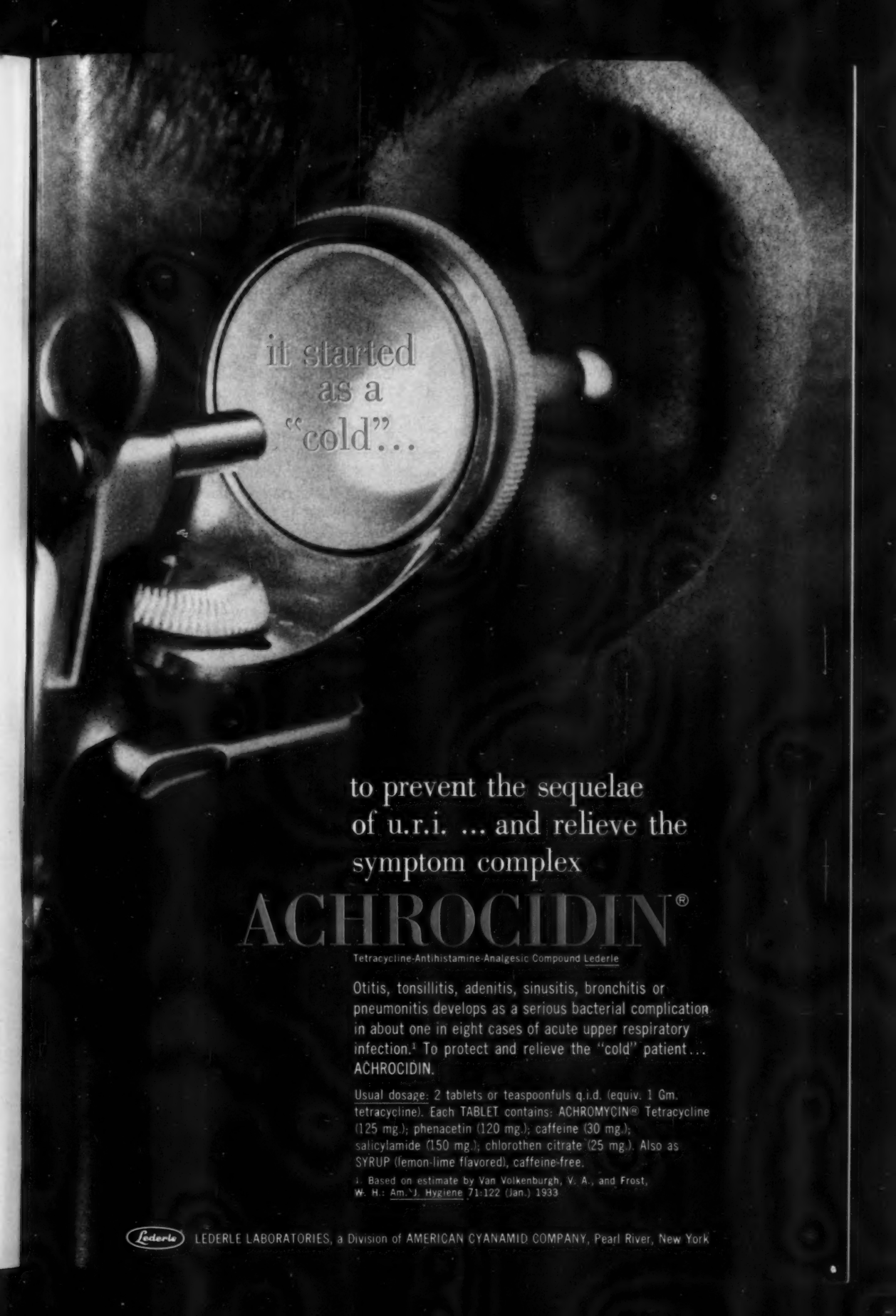
One of the obvious goals of secondary gain is monetary compensation for the injury. The law has established that illness, suffering and incapacity entitle the legitimate plaintiff to compensation in the form of money, since it is our universal medium of exchange. The patient who has a neurotic incapacity precipitated by a sudden accident may usually be considered a legitimate plaintiff. Secondary exploitation of a wealthy defendant is yet another matter, and unfortunately for the prognosis of the neurosis and equally for legal justice it is relatively easy to rationalize. This capability of the neurotic to become even more neurotic for practical purposes is one realistic fact of human psychology we must *all* recognize.

Davidson[4] discusses the compensation problem in these words: "In some patients the desire for cash compensation may be the major, though usually unconscious, force in keeping the symptoms alive. In workmen's compensation cases, the financial award is usually small and doled out over a long period. In tort actions, the compensation could be large (in the patient's fantasy the sum might amount to tens of thousands of dollars) and is usually paid in one lump sum. Psychologically, there is a considerable difference in the dynamics of the desire for compensation in these two groups of cases. In the workmen's compensation case, the weekly award is usually much less than the claimant had been earning, or could be earning, so that the dollars and cents value of the neurosis is negligible. However, the money has potent symbolic value. The weekly compensation check, flowing in steadily regardless of how early the patient arises or how hard he works, is a comforting symbol of security.

"The psychiatric examiner for an insurance company may testify that a desire for compensation is a primary motive sustaining the patient's symptoms. On cross-examination he may be asked:

" 'If this worker had no symptoms, he could earn $60 a week at his regular job. His maximum compensation is $25 a week. If, as you say, desire for money is the prime factor here, how do you explain his election to remain ill at $25 a week rather than to earn $60 a week by getting well?' By any rational arithmetic the decision of course is inexplicable. Actually, however, the patient gets more than $25 a week; he gets sympathy and attention; he

(Continued on page A-60)



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1. Based on estimate by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1933

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avoids a possibly disagreeable job; he has the assurance of a steady income regardless of what happens to him. Furthermore, the motivation is rarely anything as simple as an uncomplicated greed for money. Some claimants derive unconscious satisfaction out of punishing the employer. Some have lived for years in fear of losing a job, and the weekly compensation check is satisfyingly independent of employment fluctuations.

"In tort actions, the mechanism is somewhat different. Here the possible cash award may look to the patient like a veritable fortune. A $30 a week laborer dreams of getting, perhaps $50,000 and damages. That will set him up in his own business. He develops the fantasy of 'being his own boss' and of the snowballing earnings which his business will yield. He usually allows, in his own thinking, for the persistence of his disability. If, for example, he has a hysterical paralysis following the accident, the fantasy includes a picture of himself sitting in a wheel chair as he operates his own business. This concept is essential to preserve his sense of his own honesty. Unless the wheel chair were a permanent part of his future, the large cash award could not be justified. This differentiates him from the malingerer."

The idea is prevalent that once compensation is paid, the symptoms vanish and the neurosis is cured. This may happen occasionally, but I personally know of no such case. If the patient has a neurosis, the unconscious turmoil and conflict are not so easily disposed of. The desire for compensation, being a part of the secondary gain, is not the core of the neurosis.

This vexing problem of compensation may be clarified by a couple of case illustrations:

A 40 year old plasterer fell 6 ft. from a scaffold, landing with most of his weight on one heel. The only demonstrable physical damage was a linear crack in the os calcis. He was emotionally shaken by the unexpectedness of the fall. He immediately experienced tension, anxiety and weakness in both legs. As the weeks went by he was unable to return to work because of shooting pains in both legs, generalized weakness and an upset stomach. Examinations by his family doctor and a neurol ist were negative. Two years later this man was still unable to return to work because o leg pains and weakness. His history indicates hat he has always been an inadequate person He did not complete the eighth grade and had worked all his adult life as a laborer. He did not marry, preferring to live with and be taken care of by his widowed mother. He was adept at exploiting his more successful brother for loans, clothing, and help in procuring jobs. This ineffectual, dependent man has leaned on someone all his life. At present he is "leaning" on the insurance company for weekly workmen's compensation checks.

A 60 year old laborer poured hot tar on his arm while tarring a cement tank. Secondary infection set in and he was hospitalized for two weeks. He became tense, tremulous and restless, and complained of a variety of uncomfortable sensations in the healed scars. The hand of the affected arm was subjectively weak without objective neurologic findings. A year later skin grafting improved the function of the arm and hand slightly, but the patient was so tense and apprehensive that two months' persuasion and exhortation had been necessary to get him on the operating table. Eighteen months after the injury he was still too weak, tense and restless to return to work. The insurance company closed the case with a lump sum settlement, but six months after that the patient was tense to the point of disorganization and his hospitalization was indicated.

This man's history indicates that within the year before the accident his wife had divorced him, his son had left home to enter the army, and his daughter had married. In effect, he had no solid, stabilizing influence left in his life except his job. For 10 years he had worked satisfactorily for the same contractor. The accident, by incapacitating him for work, had robbed him of his one important psychologic support, and he gradually went to pieces.

In both these cases a legitimate neurosis developed following an industrial accident. The trauma in each case found fertile soil for the growth of severe incapacity, much of it in "secondary gain." In the first case, particu-

(Continued on page A-62)

If you were to examine these patients

could you detect the asthmatic on Medrol*?

Probably not. Not without a history.

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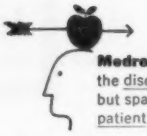

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larly, the man's basic inadequacy was a more important factor than the precipitating accident in keeping the symptoms active. In the second case, loss of family and home undoubtedly contributed to the disability for which the insurance company had to pay. Yet on the day before the accident each man was employable and employed, and subsequent to the accident each man was the loser financially by living on a compensation check considerably less than his salary. What is the proper compensation in such cases?

I would like to summarize my remarks by pointing to some of the difficulties the psychiatrist, or at least this psychiatrist, has in reconciling his experience and concepts with those of the law. It seems to me there is a basic conflict between psychiatry and the law which I find difficult to grasp but which is in part exemplified in the subject matter of traumatic neurosis. One aspect of this conflict, as I see it, is that the law has its own concept of human psychology and its own ideas of why people behave as they do. This psychology of the law is a common-sense psychology of ancient vintage and clashes at many points with the somewhat more accurate, scientific, dynamic psychology on which modern psychiatry is based.

Another aspect of the conflict is the law's seeming insistence on black or white, all or none, yes or no. There are exceptions to this, and shades of gray are occasionally acknowledged by courts. However, I have been nonplussed many times when testifying in court or before a workmen's compensation commissioner when asked, "Does this man have a traumatic neurosis?" This paper presents a few of the reasons why that is a difficult question to answer.

In some cases the patient was making a fairly stable adjustment before experiencing what was for him a severe psychologic trauma, following which persistent neurotic symptoms incapacitated him. In such cases it is relatively easy to state that the patient has a neurosis, that he has not previously, to my knowledge, had a similar reaction, and that the onset of symptoms coincided with the accident which occurred on such and such a date. This adds up to the legal concept of traumatic neurosis. In other cases the predisposition to neurotic breakdown is grossly apparent and in some instances the patient has had a previous neurosis from which he had made a symptomatic recovery. In still other cases the exploitive, secondary-gain aspect almost obscures the diagnosable primary neurosis.

Human behavior is complicated and at times baffling. The motivations for behavior, normal *or* neurotic, are multiple, intricate and often hidden. Current psychiatric concepts, a sampling of which are presented here, can be of help in understanding psychologic reactions to injury. The better we understand, the better we can conceptualize, categorize and treat.

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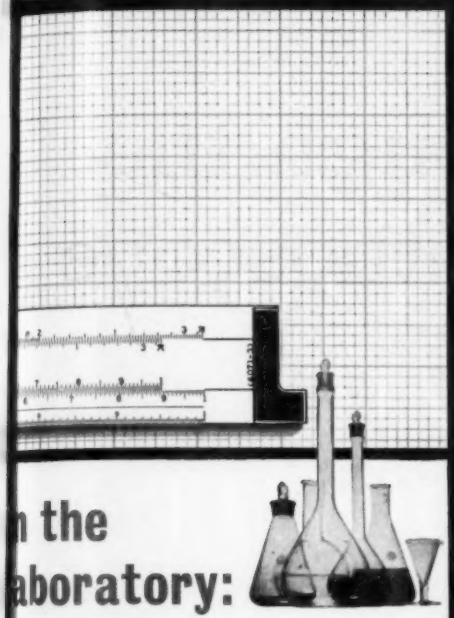

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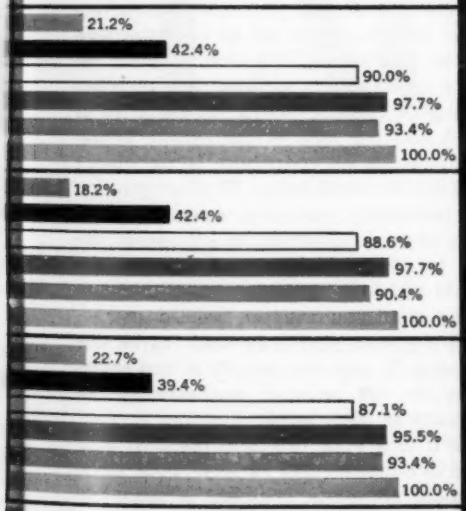

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References: 1. Koch, R., and Asay, L. D.: J. Pediat., in press. 2. Leming, B. H., Jr., et al.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 3. Meilman, et al.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 4. Olansky, S., and McCormick, G. E., Jr.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 5. Shubin, H., et al.: Antibiotics Annual 1957-1958, New York, N. Y., Medical Encyclopedia, Inc., 1958, p. 679. 6. Isenberg, H., and Karelitz, S.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 7. Wennersten, J. R.: Antibiotic Med. & Clin. Therapy 5:527 (Aug.) 1958. 8. Kaplan, M. A., and Goldin, M.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 9. Truant, J. P.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958.

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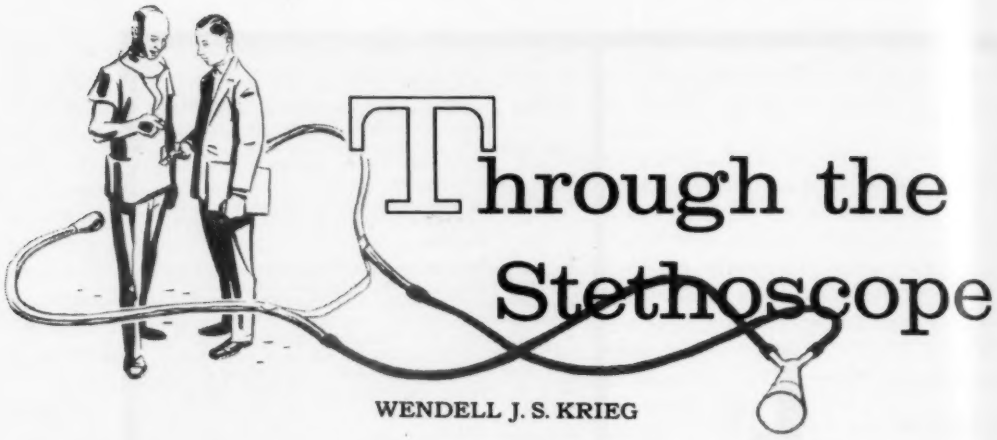

Through the Stethoscope

WENDELL J. S. KRIEG

Letters to a Medical Student

My dear son:

Your second year of medical school is coming rapidly to a close, and we are looking forward to seeing you before you go back for summer research. It will be a relief and antidote from so much study of the known, once you have had a little rest. The remainder of your life will be an alternation of the pursuit of the known and the unknown anyway.

In the lives of most professors in modern medical schools, time spent in research is about equally balanced with time in teaching. I believe this is a better arrangement than to spend full time in research, at least for most temperaments. A period of several years in the middle of your career, when familiarity with your subject makes the ramifications of your problem overwhelming and committee and other obligations are being piled on simultaneously, can profitably be taken for full-time research. Indeed, I would propose that medical schools establish rotating research institutes for productive professors, who may be withdrawn from teaching for a period of four or five years and provided with space and facilities to expand their research programs. At the end of that period, there would be a large accumulation of observations to digest and write up and plans enough for years of future work. They would then return to teaching with wisdom and renewed vigor.

Yet, paradoxically, if you take a full-time research position as a definitive appointment for life, you are sowing the seeds of unhappiness, particularly if you have been used to teaching. A continued intensive application to subjects that do not yet exist breeds tension. The patience required in amassing evidence, the intellectual isolation of most researchers or research groups, the constant sharpening of the discriminative faculties of the mind and the lack of immediate appreciation of results all contribute to unbalance equilibrium and well-being. If your position is in a university, you are separated from students, and you don't fit in with your colleagues, for they disdain or envy you for having no teaching duties and are likely to show you that you are no "sacred cow"—when all the time you only want to be one of the boys. If you are not in a university, you may be too isolated intellectually for good results in such work.

Worse it is if your full-time research is of the pure or fundamental variety. Your isolation is more complete, criticism is more rife and less answerable, and your very continuation is jeopardized. Any research is already once removed from the practical and, until

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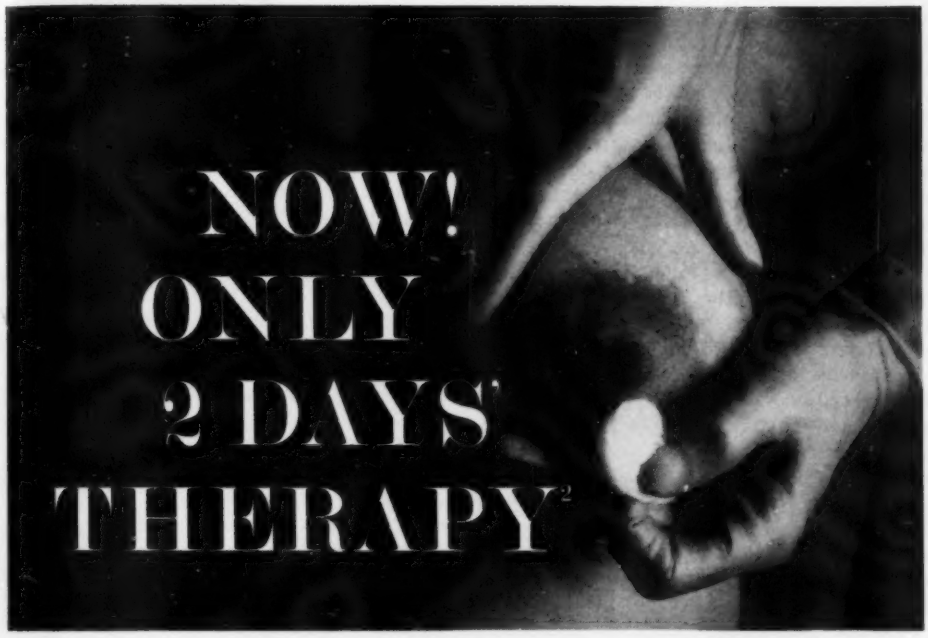

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recently, has had difficulty enough in making its way. You can get a living from it, but rarely a good one. Indeed, you can take it for a working axiom that the world will not pay for philosophy, poetry, pure mathematics or fundamental research. When a researcher is turning out work that others can use directly, he sometimes finds a measure of general toleration; when he is on basic research, he is shaky; but when he becomes philosophical or just writes, he is on the way out. Administrative practice has shown that no research professorship is sacrosanct, but in a teaching post the teaching always has to be done.

Do not be dismayed by your fellow medical students who talk about service to suffering mankind. If they only care to step aside, there are plenty of others to take their places, so they need not feel they must make a sacrifice. You can test the purity of their desire for service by determining their willingness to enter research and teaching. Volunteers are really needed here. John Martin used to say the practitioner is a parasite on science.

I do not recommend that your prime motive for doing research necessarily be that of benefiting mankind. This justification can be reserved for appeals for funds and popular addresses. Then what should motivate your research? Most of the strange things with which men occupy their lives are for money. No one in his right mind would enter research in the medical sciences for this purpose. Some do research to obtain academic preferment and stop when they have a full professorship; others do it to obtain approbation of their colleagues and achieve their envy or hatred. Still others want to obtain a place in the history and literature of their subject and in the memory of posterity, forgetting how soon all but a few become lost in the literature or are succeeded by more definitive work. Best of all, however, is it to investigate because you yourself are interested in obtaining an answer to a problem and enjoy the process of finding it.

Do your research for your satisfaction, not to appeal to or impress others. Your publications ought to be a series of worked-up notes, furnishing a basis for future extensions. Your work should be the unfolding of the inner bud of your intellect, and it is only by permitting the outer leaves to expand, flourish and drop away that the flower can develop fully and naturally. Only this inner bud is of value; everything else is for its nourishment. As in nature, leaves are everywhere, but the specificity and the value is in the flower. It is the flower that sets the seed.

You will have to go through many stages of effort to develop something new. Yet, if this flower is not matured, the leaves are in vain. However, many fertile minds are nipped in the bud today, like broccoli or cauliflower, and stewed in the administrative soup.

Don't let your love of fascinating detail tempt you to abide long in the pleasant but overfurnished and overheated drawing rooms of worked-out science, attempting to squeeze in a piece of bric-a-brac here, a miniature there. Find yourself a spacious and unfurnished hall. It will be drafty and your own voice will echo at first, but you can furnish it and make it your home.

Don't be a science "hitchhiker," forever the end man on somebody else's papers. The best-known person will get all the credit, even if the idea and most of the work were yours. Too many are crowded in the halls of learning today for you ever to raise your voice above the multitude otherwise. Everyone is constantly besieged by names of persons, from Abercrombie to Zurbrigen. We must be like a telephone directory, responding with the right number. "Oh, yes, he was the man who . . ." We all like to have a handle to lift things. People who are not associated with some achievement are like a hot kettle of which the bail has fallen down.

I don't want to give the impression that you will enjoy glory. This rarely comes to the research man except to Nobel prize winners and "blue baby" surgeons. Any satisfaction must be an internal glow, which it is not good taste to communicate. You will work hard for years before anyone, except a few friends, knows who you are, and the chances are against any tangible reward other than the gradual, expected rise in your profession as you get older.

I am glad that you are receiving good grades in pathology. It would be a mistake to allow your decision to induce you to fall down in that subject, which is the nodal science where all preclinical studies meet, and from which all clinical subjects branch out.

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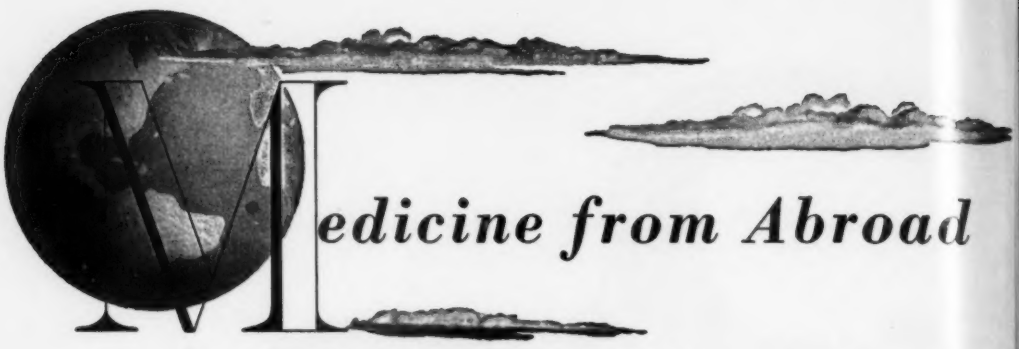

Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

AUSTRIA

Sickle cell disease—In discussing sickle cell disease at a meeting of the Vienna Society for Internal Medicine, Dr. Julius Bauer, Professor of Internal Medicine, College of Medical Evangelists, Los Angeles, reported that although anemia is the most frequent and outstanding manifestation of the disease it is not always present. Impairment of peripheral circulation by the obstruction of small blood vessels is the most important, dangerous and, often, misleading clinical symptom.

Sickle cell disease is interesting because it demonstrates that a genetically determined substitution of a single amino acid (glutamic acid) by another (valine) among the approximately 600 amino acids of the globin fraction of hemoglobin is the basic difference between sickle cell (S) hemoglobin and the normal adult (A) hemoglobin. Thus, this single mutant of one amino acid of the hemoglobin molecule is responsible for the variable clinical picture with its different symptomatology. Karl Singer has shown that the fate of a carrier of S hemoglobin depends on the quantity of S hemoglobin in the total blood mass, which is low (23 to 45 per cent) in heterozygous carriers and high (76 to 98 per cent) in homozygous carriers.

Complications of hemophilia—Dr. F. E. Matt presented for demonstration a patient who had had hemophilia B for some time. The patient had repeated episodes of severe bleeding in his joints, and his knee joints had become ankylotic. Eight days before admission to the hospital he received a blow to his right upper arm in a fist fight. Although no bleeding occurred immediately after the injury, 48 hours later his right arm began to swell; the swelling continued to increase after he was admitted to the hospital. In spite of the liberal use of blood plasma and whole blood, the hemorrhaging did not stop, and cutaneous necrosis developed due to the pressure of the large amount of blood in the subcutaneous tissues. Spontaneous perforation of the necrotic skin revealed a blood coagulum larger than a man's fist.

In discussing the case, H. Deutsch observed that long-lasting effects are usually obtained when plasma or whole blood is given to patients who have hemophilia B. This case was an exception. Although the amount of plasma and whole blood initially given was ineffective, more intensive treatment might have prevented the increased bleeding. It is essential to maintain therapeutic blood transfusions until healing is complete. Even if hemorrhages do not occur, the rate of healing will decrease when the blood transfusions are discontinued.

In treating internal hemorrhages a special problem arises. When large amounts of plasma are given, the patient is endangered by excess fluid; on the other hand, administration of double-concentrated plasma for a longer period results in exsiccation of the tissues. A suitable compromise must be found.

H. K. Kundratitz advised a more active procedure in the case presented, since there was risk of necrosis. However, the surgical consultant was afraid that surgery would cause uncontrollable bleeding, and he would not operate until the blood coagulum was exposed by cutaneous perforation. Hemorrhage did not occur when the coagulum was subsequently removed, and the wound healed without complication.

(Continued on page A-86)

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References:

1. Shapiro, S.: Observations on the use of meprobamate in cardiovascular disorders. Angiology 8:504, Dec. 1957.
2. Friedlander, H. S.: The role of ataraxics in cardiology. Am. J. Cardiol. 1:395, March 1958.
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Globe cell anemia—An 11 month old girl who was admitted to the hospital because of a hemolytic crisis was found to have constitutional globe cell anemia. The child had had typical severe jaundice in the newborn period. Her mother also had globe cell anemia; however, serologic tests excluded the possibility of blood group incompatibility. In describing this case, H. H. G. Wolf emphasized that globe cell anemia must be differentiated from other types of neonatal and infantile anemias.

BRAZIL

Maurer's cavernostomy—In *Revista paulista de medicina*, Amaury Louzada Velloso lists the indications for Maurer's cavernostomy, describes the factors contributing to good results, and presents a series of technical data useful in local treatment of tuberculous cavities of the lung. The favorable results reported by the author place this method among the sanctioned procedures of treatment. He condemns the palliative methods which have tended to discredit cavitary drainage.

Varicose veins—In the same journal, a follow-up of operations on varicose veins in the limbs was reported by Puech Leão, Martins de Toledo, Irany Moraes, Bueno Net, V. Khouri and C. O. Bellio. An analysis of recurrences and their possible relation to the surgical technic used showed that permanent good results can be obtained only if very extensive and radical surgery is performed. The various steps of this procedure, which are described in detail by the authors, include: (1) high ligation and division of the great saphenous vein or the small saphenous vein, or both, with ligation of all collateral branches at their juncture with the deep vein; (2) ligation of all incompetent communicating veins; (3) stripping of all varicose veins which are straight enough to allow passage to the stripper; (4) removal by direct dissection and by evulsion through multiple small incisions of all varicose veins which are too twisted to be stripped; and (5) subfascial ligation of the communicating veins of the lower third of the leg in patients with induration of the skin and subcutaneous fat.

Hypospadias—In *Revista paulista de medicina*, Geraldo Campos Freire, Roberto Farina, S. Seraphim and Oswaldo de Castro presented their conclusions on the embryology, symptoms, signs and varying degrees of hypospadias. They found that when these malformations occur in the male, the curved penis must be corrected using Blair's technic, before the hypospadias is repaired by the Leveuf technic, also known as Cecil's or Cabot's technic. In the authors' opinion, urinary diversion need not be made. Choice of time for the operation is also considered.

Bronchitis—In discussing the interrelation of bronchitis and bronchial asthma in *Laboratorio clinico*, Alvaro Murce noted that acute primitive bronchitis occurs more often in children than in adults, and that prophylactic measures and treatment with antibiotics and sulfonamide compounds have reduced the incidence of bronchopneumonia and bronchiolitis.

He points out the close connection between spasmodic bronchitis and asthma, and, while he makes a clinical distinction among spasmodic bronchitis, asthmatic bronchitis and bronchial asthma, he believes that etiologically and pathogenically they are a progressive series of the same disease. Spasmodic bronchitis and asthmatic bronchitis are considered a sole entity by some authors. Nevertheless, differences do exist in manifestations of these bronchial conditions and in their characteristic periods of occurrence in certain age groups.

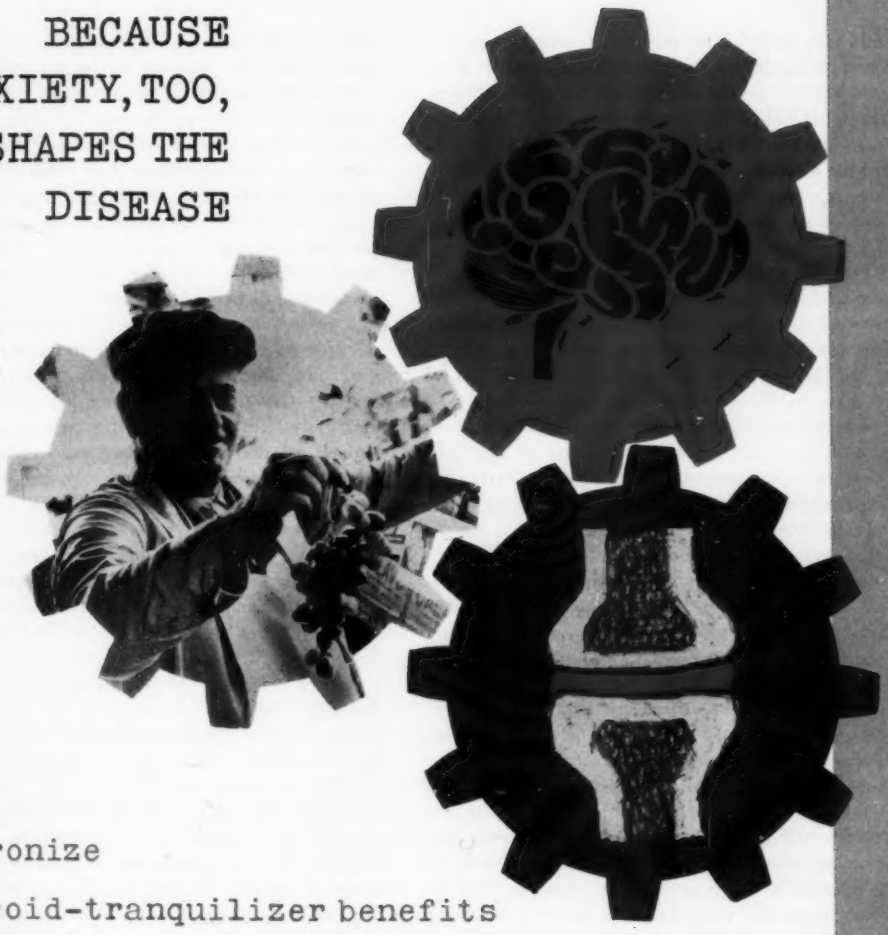
Heredity and constitutional factors, particularly exudative and neuropathic diatheses, which predispose the patient to bronchitis and other respiratory disease are considered. These conditions are nearly always coexistent and are usually seen in young patients. The author also discusses the action of the allergic factor and the infectious elements, which often are present in the same patient.

ENGLAND

Genetic hazards of radiation—A symposium of eight articles dealing with radiation hazards has been published in the *Practitioner*. Dr. Alan C. Stevenson, Medical Research Council Human Population Genetics Research Unit, Oxford, contributed an important article on the genetic hazards of radiation. Our understanding of the nature and, particularly, of the quantitative aspects of genetic damage from

(Continued on page A-88)

BECAUSE
ANXIETY, TOO,
SHAPES THE
DISEASE



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radiation is still very meager. Nevertheless, it is perhaps significant that four major reports from groups of scientists in England, the United States, the World Health Organization and the United Nations Assembly have shown surprising unanimity in their conclusions as to the limited deductions which can be made from the knowledge currently available.

After examining the evidence, we must conclude that all ionizing radiations increase mutation and that the over-all effect cannot be considered as other than harmful. It follows that every possible step must be taken to reduce the amount of unnecessary exposure to individuals and groups. Since in our own society diagnostic radiology contributes much more man-made exposure to people less than 30 years of age than does any other means, doctors have a particular responsibility. Clearly the interests of the individuals who require diagnostic x-rays are to some extent in conflict with the interests of future generations—of individuals whose ancestors the former may be, but who will have hundreds or even thousands of other ancestors. Even considering the conflicting interests of patients, however, apparatus can be designed, maintained and used so that a minimum of stray radiation reaches the gonads, and the gonads often can be shielded. No experienced doctor would maintain that the number of exposures per person could not be reduced by avoiding repeat exposures when past records can be obtained and by using x-rays only when they are essential to the patient's interest. The radiation received from diagnostic x-ray is much more relevant to future generations than to the present one; individual dosages are small, but many people—eventually the whole population—will be exposed. The ages of patients exposed are important when subsequent childbearing is considered. A few procedures requiring abdominal fluoroscopy or repeated radiography contribute a considerable proportion of the total exposure received by the population. The chances, however, that the immediate offspring of any person exposed even to therapeutic doses would be affected in any way are extremely small and can be ignored. There is far less danger with diagnostic exposures.

Headache and gastric evacuation—At a discussion at the Royal Society of Medicine, Dr. L. S. Carstairs, radiologist to the Royal Northern Hospital, London, pointed out that headache, particularly of the migrainous type, is often associated with a delay in gastric evacuation. The subject does not appear to be generally recognized today, although as long ago as 1929 Sir Arthur Hurst, the well-known London physician, said that he had saved several patients from undergoing an operation for supposed pyloric obstruction when they really had migraine.

The physiology of migraine, headache, nausea and vomiting is complex and not fully understood, although the mass of experimental and observational evidence relating to the control of gastric activities has been well summarized by Alvarez in his "Introduction to Gastroenterology." The migrainous stomach most closely resembles the stomach following vagotomy. The acts of retching and vomiting do not necessarily depend on distention of any portion of the alimentary tract, although they can be induced by such distention or by the instillation of noxious substances. Nausea is a subjective sensation which can be initiated through many pathways, both central and peripheral. Delayed gastric evacuation is not always associated with nausea. It must not be forgotten that patients may have both migraine and peptic ulceration.

Effect of alcohol on a skill resembling driving—In spite of extensive literature on the subject, very little precise information is available at present about the physiologic effects of alcohol and about its effects on behavior. This is especially true of the effects of smaller doses of alcohol. Miss Hazel A. Long, Mr. G. C. Drew and Dr. W. P. Colquhoun, department of psychology, Bristol University, have published an important study in the *British Medical Journal* on the effect of small doses of alcohol on a skill resembling driving. Their aims were to relate any changes found to the level of blood alcohol; to see whether different individual responses to alcohol could be explained in terms of previous experience or of temperamental differences, when every effort had been made to minimize differences in blood alcohol level; and to investigate the accuracy of estimating blood alcohol level by measuring the alcohol excreted in urine and in breath.

An apparatus known as the Miles motor-driving trainer was employed, in which the subject sits in a dummy automobile, facing a translucent screen in a darkened room; a road scene painted on a transparent disk is greatly magnified and projected on the screen. As the driver operates the accelerator and steering wheel to

(Continued on page A-90)

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change his speed and direction of movement, the automobile appears to progress along the road. The effect is reasonably realistic, and experienced drivers have little difficulty with it.

Thirty-five men and five women from the staff of the Road Research Laboratory volunteered for the test. All were in good health and held driving licenses; with the exception of one person, aged 58, their ages ranged from 23 to 40 years. The majority reported that they took alcohol only occasionally. The alcohol was administered orally as absolute alcohol diluted to a 20 per cent solution and flavored to disguise the alcohol content. The aspects of performance measured were the accuracy of tracking, the speed at which the task was done, and the operation of the controls. Tracking error showed very little change with practice, but there was a progressive increase in speed of driving throughout the experiment. Accuracy of steering decreased progressively as the blood alcohol increased, even with the low concentrations used in this experiment. Blood alcohol concentration showed a characteristic change with time after drinking, showing a steep rise to a maximal value, followed by a slow return to normal.

The present study showed that performance began to deteriorate with very low blood alcohol concentrations (certainly with those of 20 to 30 mg. per 100 ml.), and that the deterioration was progressive and linearly related to blood alcohol level. No evidence of a threshold effect was apparent in this study.

The impairment of performance was shown most clearly in the operation of the controls. As the aim of the task was primarily to track, it was perhaps not surprising that in attempting to retain a level of accuracy the operation of the steering wheel was most affected. Efficiency in using the steering wheel was indicated by the amount of tracking error which resulted. With practice the amount of steering wheel movement decreased without a reduction in the accuracy of tracking, whereas after the administration of alcohol, tracking error increased despite an increase in steering wheel movement. This suggests that timing of the steering wheel movements was upset. The decrease in consistency of movements required to turn a corner supported this view.

Age, sex, previous driving experience, and previous drinking habits, within the limits available, showed no relation to individual differences in response to alcohol. Personality ratings, especially those relating to extraversion-introversion, showed a definite relation to behavior change. Extraverts did not change either speed or control movements very much; however, they were less consistent in control movements and showed large increases in error. Introverts changed speed considerably, although it was not possible to differentiate between those who decreased speed and those who increased speed. Control movements also increased, but were relatively consistent. Error may or may not have increased, but the mean error score was significantly less than that for extraverts.

FRANCE

Reactions to BCG vaccination—Children's reactions to BCG vaccine have been studied by Dr. Mande and associates at the International Center of Childhood, an institution created by American funds. Results of this study were published in *La semaine des hôpitaux de Paris*. The initial investigations were conducted at a time when newborns were given small, orally administered doses of the vaccine; tuberculin reactions were changeable, ephemeral and of weak intensity. (The same reactions were observed in experiments with calves and guinea pigs.) In less than two years, reactions in the majority of patients became negative. If patients were not revaccinated, strongly positive reactions or positive reactions after several years were considered indications of superinfection with Koch's bacillus.

These early concepts have been modified as a result of new methods of vaccination, including the intradermal inoculation of Wallgreen, the multiple scarifications of Nègre and Boquet, the multiple injections of Bukhaug and Rosenthal, and the large, orally administered doses of vaccine used by De Assis.

The sensitivity, which is almost always definite and of several years' duration, and the spontaneous allergic symptoms of primary infections may be compared on three bases: (1) the diameter of the local red spot, which varies from 6 to more than 30 mm., (2) the diameter of the swollen area, and (3) the type of infiltration, which is more or less homogeneous and distinct to touch. Infiltrations are labeled according to

(Continued on page A-92)

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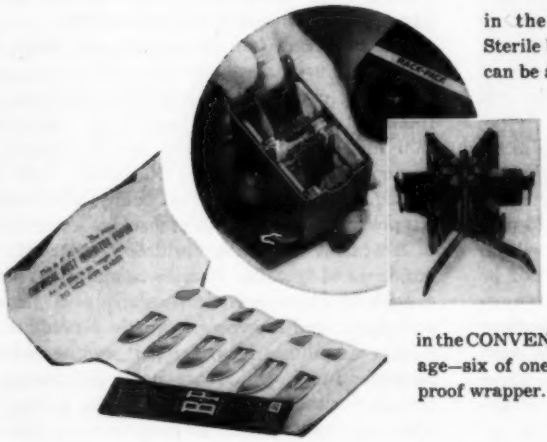

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the four degrees of Palmer and Edwards, which are somewhat accurate despite their subjective nature. These manifestations are difficult to study, except by means of the intradermal (Mantoux) test, using 0,1 ml. of fluid.

Following the BCG vaccination and in primary infections three-fourths of the reaction areas are 10 to 20 mm. in diameter; the area, degree of homogeneity, and consistency of the infiltrations are comparable. Statistics show that strong reactions over 30 mm. in diameter occur in 25 per cent of patients with primary infections and in 10 per cent of persons vaccinated with BCG; vesicular reactions are very rare. However, in spite of the statistics, distinction in specific cases is impossible. The majority of studies indicate that time reduces the intensity of reactions to BCG, manifested first in the consistency and homogeneity and later in the diameter of the red area. After four years, the reaction from any type of vaccine will be negative in about 20 per cent of cases. Such negative reactions have been verified by BCG tests. In these instances the patients were revaccinated and their reactions were again positive. Since none of the patients manifested Koch's phenomenon, the positive reactions indicated the presence of an unrecognized allergy.

That this process of attenuation does not always occur has been confirmed by the 16,500 vaccinations performed by Gernez-Rieux in France and by Danish and Swedish studies which have shown numerous cases in which reactions to BCG vaccinations have become stronger rather than weaker. In some patients, the diameter of the reaction area gradually increased from 7 to 8 mm. in a period of eight years.

There is no satisfactory explanation of these observations. The divergent reactions may be attributable to the fact that different lots of the vaccine vary in strength and the tendency to provoke a violent tuberculin reaction. Even within the same lot, the tubes of vaccines may not be identical. There are also individual differences in patients. Regardless of race, all people show the same tuberculin reactions; however, in each group some patients are easily sensitized, while others show continued negative reactions. It has been noted that in all statistical series 5 to 10 per cent of sick students become sensitized only after repeated inoculations.

Markedly positive reactions have been observed in children long after BCG vaccinations. In one instance such reactions in the course of a febrile disease were erroneously diagnosed by the physician as indications of primary infection.

Annual intradermal tests are necessary after BCG vaccinations. Primary infection is indicated only by a sudden and marked reaction to intradermal tuberculin tests. Since a moderate and gradual increase in the diameter of the reaction area can follow inoculation, only a massive and blunt increase should be considered suspicious. The BCG vaccine protects against contamination by the virulent Koch bacillus, but there may be some bacilli of exceptional virulence.

SPAIN

Moniliasis—Dr. Garcia Orcoyen, director of public health in Spain, presided at the first national colloquy on monilial infections, held in Madrid. The meeting, which was attended by physicians from various countries, was organized by Dr. Quintana, former director of public health at Madrid and counselor of the National Institute of Social Medicine. Dr. Edouard Drouhet, chief of the mycology service of the Pasteur Institute in Paris, reported on "Pathologic and therapeutic aspects of 'bandidiasis.'" Other papers were read by Drs. Bedoya, Gomez Organeja, Botella Llusia and Gomez-Jiminez de Cisneros.

The occurrence of undesirable side effects following the use or overuse of antibiotics is an increasingly common problem. The symptoms and treatment of conditions caused by administration of antibiotics and the special dangers to young children caused by the drugs were discussed. It was reported that orally administered streptomycin is one of the most dangerous forms of treatment for young children. Apparently the incidence of monilial diseases in children reaches a peak in December, drops sharply in January and April, and increases again in November.

In a round-table discussion it was agreed that parasitic fungi, which are normally present in certain organs of the body, become pathogenic when a condition such as pregnancy or diabetes lowers the body's resistance. Due to the present widespread use of antibiotics, the normal flora of the body becomes displaced, and monilial disease appears as a clinical manifestation. A new therapeutic agent, MYCOSTATIN®, has been found effective against many monilial conditions.

Esophageal dysfunction in an infant or child usually results from congenital or traumatic lesions or chemical burns. Congenital conditions include benign strictures and webs, a short esophagus and atresia. The swallowing of foreign bodies and chemicals accounts for most of the traumatic lesions. Cardiospasm and esophageal varices are relatively uncommon in children; however, esophagitis occurs frequently. The authors discuss the diagnosis and treatment of each of these conditions.

Esophageal Diseases in Infants and Children

KENNETH C. JOHNSTON* AND PAUL H. HOLINGER†

University of Illinois College of Medicine, Chicago

DISEASE of the esophagus in infants and children comprises chiefly congenital lesions, traumatic lesions—due to either foreign bodies or perforation by instrumentation—and, finally, chemical burns caused by the ingestion of caustics or corrosives. Some of the esophageal disorders commonly seen in adults, such as cardiospasm, esophagitis and varices, are occasionally encountered or their presence suspected in the younger age group, and necessitate investigation and therapy. Neurogenic disorders of the swallowing mechanism are not uncommonly seen in newborn infants, either as a result of slow development or associated with hydrocephalus and other diseases of the central nervous system. Accepting these as extra-esophageal lesions, the resulting esophageal dysfunction deserves special consideration and study.

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KENNETH C. JOHNSTON

PAUL H. HOLINGER

Facilitation of diagnosis and treatment of esophageal disease in early life has been obtained through the improved methods of endoscopic and roentgenologic examination, a more concise understanding of the indication and limitation of conservative therapy, and the evaluation of some of the end results of comparatively new surgical technics. In many instances, careful observation and timely attention will lead the clinician to suspect the presence of esophageal disease and permit early diagnosis and treatment. A deviation

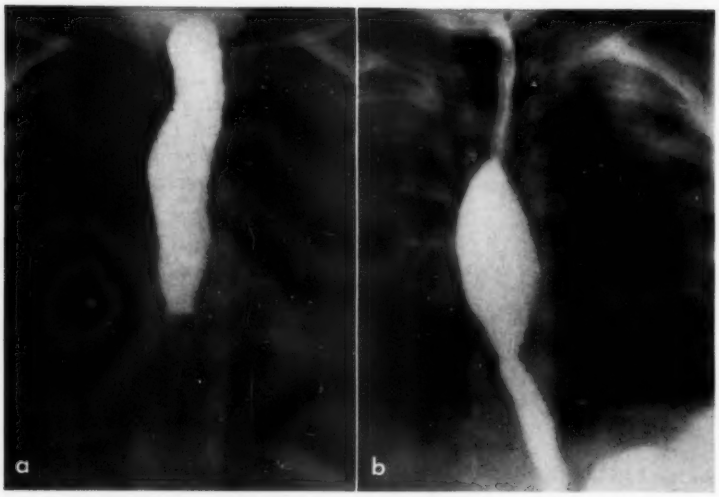

FIGURE 1a. Congenital stricture of esophagus in a 15 month old boy. A foreign body (pea) is present in the distal portion of the esophagus. b. Appearance of barium column after removal of the foreign body.

from the normal feeding pattern or swallowing function in an infant or a small child deserves at least the benefit of an esophagram. Frequently, the difficulty appears at four to six months of age when the infant is first given semisolid food. The feeding time is prolonged and the food may even be rejected. The change in feeding habits is often considered the beginning of an altered behavior pattern, and, as the child grows older, valuable time may be lost in attempting to treat the condition on a psychogenic basis rather than by first ruling out the presence of an organic lesion in the esophagus.

Benign Strictures and Webs

The most common congenital lesion is benign stricture. Frequently, the abnormality is first noticed when the infant begins to take solid food. The symptoms vary in intensity, depending on the severity of the stricture. The infant may take a long time for the feeding,

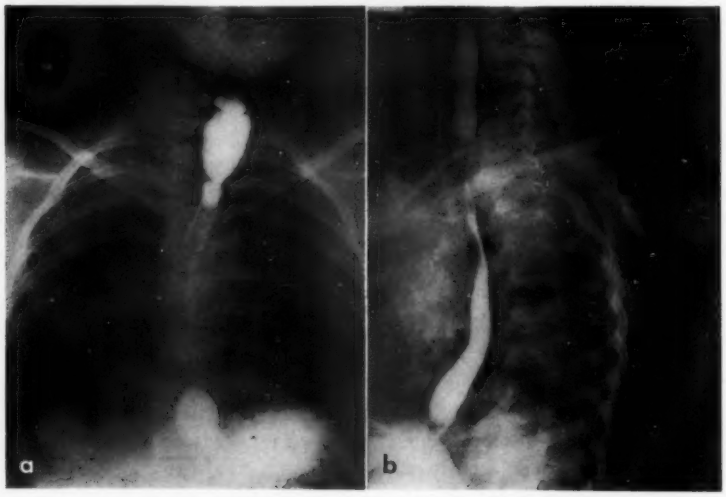

FIGURE 2a. Esophageal webs in an eight year old boy who had had dysphagia for solid foods since he was two years old. b. Dilatations with the esophagoscope and bougies resulted in a remission of symptoms.

or, if the stricture is more severe, the infant may regurgitate the food, or complete obstruction of the esophagus may occur. Occasionally, the presence of a foreign body which would cause no difficulty in a normal infant may be the first indication of the stricture[1] (figure 1).

In those instances in which the stricture is severe, a history will be obtained of slow feeding or regurgitation of feedings since birth. Rarely, the patient will reach adult age having had occasional episodes of choking, but none so severe that medical attention was sought. Then a bolus of meat will become lodged in the stricture and necessitate removal, and the true nature of the condition will be determined.

The stricture will usually be in the distal third of the esophagus, but may be found at any level. It may be constituted by a partial or complete web (figure 2) or may be a fibrous stenosis occupying a varying proportion of the length of the viscus (figure 3). The site, distribution and severity of the lesion can be portrayed by an esophagram. In all cases except those in which the stricture is severe and choking and gagging may lead to aspiration of the swallowed medium, barium can be used. If aspiration of the radiopaque substance is a possibility, iodized oil is preferable. When a stricture is seen roentgenographically, esophagoscopic visualization of the lesion is indicated. This not only allows for inspection of the lesion but will in many instances lead to the first dilatation of the stricture. The extent and nature of the stenosis will be more exactly ascertained and the probable response to treatment may be determined. The subsequent management is, therefore, often determined at the time of this first esophagoscopy.

The instrument to be used will depend on a careful consideration of the roentgenologic appearance of the stricture and the age of the patient. The infant esophagoscope should be used in infants under one year of age. A larger tube provides better visualization and would permit passage of dilating esophageal bougies through it, but it is likely to obstruct the airway. If passage of the instrument meets with slight resistance and no other lesion is seen, subsequent dilatations may be accomplished by careful insertion of the Hurst type of mer-

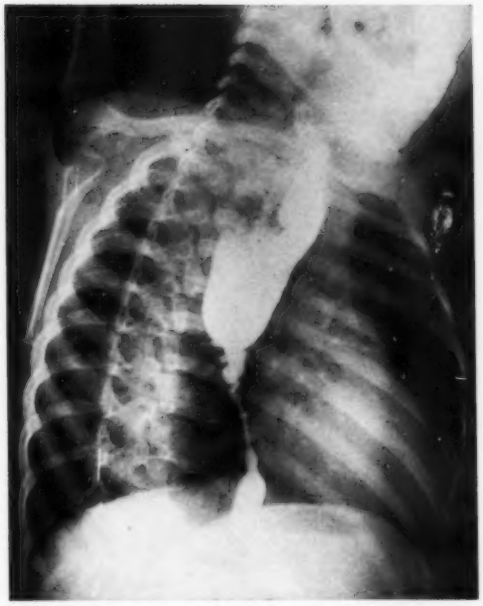

FIGURE 3. Congenital stricture of esophagus and dilation above the stricture in a four year old child.

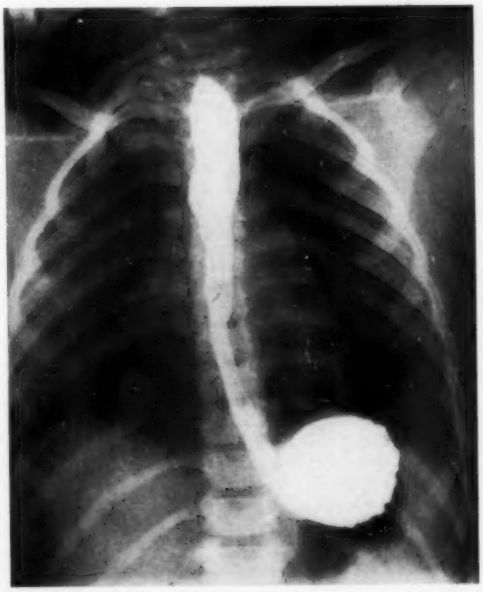

FIGURE 4. Same stricture as shown in figure 3. This roentgenogram was made when the child was eight years old. Esophagus first was dilated with the esophagoscope, and the dilatation was maintained with mercury-filled bougies.

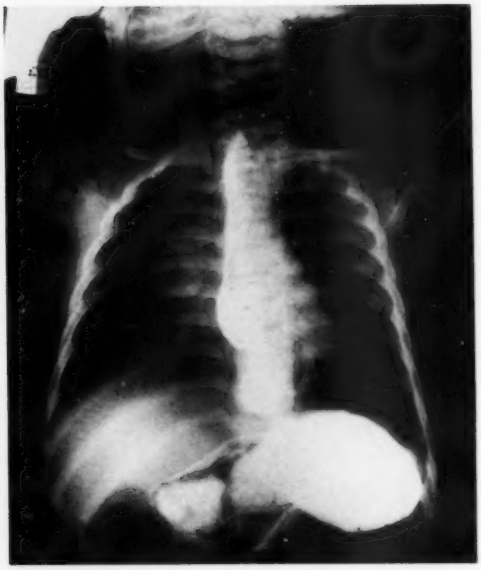

FIGURE 5. Congenital short esophagus in a six month old infant who had vomited after each feeding since birth.

cury-filled bougies at intervals of a few days to several weeks, which will be dictated by the response to treatment. In many instances, the esophagoscope may have to be passed several times before the stricture will permit passage of a flexible dilator. When a satisfactory lumen has been obtained, the dilatations are repeated as often as necessary to keep the patient symptom-free or to retain an adequate patency (figure 4).

In rare instances, a very small and very firm stricture will be encountered in early infancy. Repeated unsuccessful attempts at esophageal dilatation may show this to be a hazardous procedure. In such cases, gastrostomy is indicated for two reasons: (1) to maintain nutrition and (2) to allow for dilatation over a string. If the condition still fails to respond to this treatment, surgical intervention may be necessary, but experience has shown that surgical resection and end to end anastomosis often result in postsurgical stricture at the anastomotic site. It may then be necessary to dilate the postsurgical stricture, but, if dilatation is begun early, the response may be better than that of the original lesion. If it is at all possible, resection of the esophagogastric junction should be avoided.

The subsequent care of a congenital stricture depends on the severity of the lesion and the response to dilatation. Usually, an adequate lumen is established, and, except for an occasional episode of minor obstructive symp-

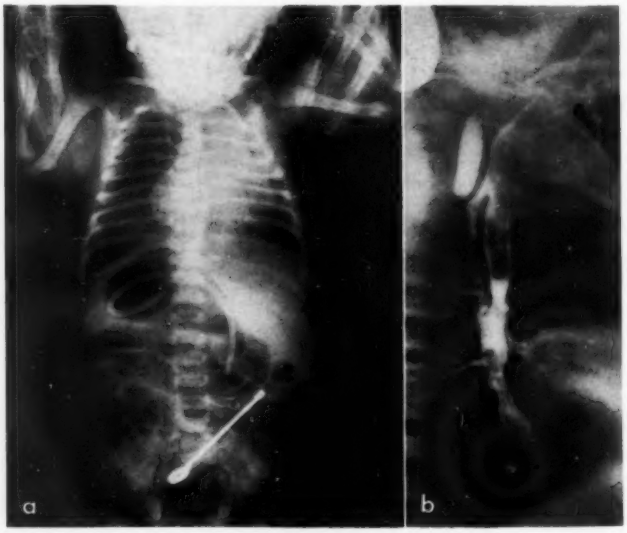

FIGURE 6a and b. Congenital atresia of the esophagus and a tracheo-esophageal fistula. A feeding tube passed into the stomach erroneously tended to rule out the presence of atresia, but ingestion of Lipiodol revealed the true nature of the anomaly. The feeding tube had passed through the trachea and into the lower esophageal segment.

toms after a hastily swallowed meal, no treatment other than observation is required. On occasion, dilatation will be necessary at intervals of one to six months throughout adolescence. Episodes of foreign-body obstruction may be encountered, and esophagoscopic removal will be necessary. The patient will appreciate his limitations in this respect and will be able to prevent these accidents by more careful mastication of his food or by observing the necessary care in his manner of eating.

Congenitally Short Esophagus

The congenitally short esophagus simulates a benign congenital stricture in symptoms and in the roentgenologic appearance (figure 5). In cases of this condition, a stricture is frequently found in the lower part of the esophagus similar to a simple stricture, but, esophagoscopically, the typical red gastric mucosa with rugose folds is observed above the diaphragm, immediately below the stricture. The lesion often presents a different problem in management from that of the simple stricture, since it is usually accompanied by a complicating esophagitis which induces esophageal spasm to increase the obstruction and offset the attempts of active esophageal dilatation. The dilatation of the distal portion of the esophagus is repeated as often as required with the rigid tube or, when possible, with soft rubber, mercury-filled bougies. Again, surgical intervention should be delayed through adolescence if possible. When conservative treatment fails, the operative procedure of choice will probably prove to be a resection of the stricture with replacement of the stomach below the diaphragm and the introduction of a portion of bowel between the stomach and lower part of the esophagus.

Congenital Atresia

In recent years, the care of congenital atresia has been an outstanding problem for the endoscopist and for the chest surgeon. In the majority of cases of atresia, a tracheoesophageal fistula is present. In most cases (93 per cent) there are a blind upper esophageal segment and a lower segment which opens into the lower part of the trachea or the left bronchus[2] (figure 6). Fortunately, this type can be successfully treated surgically in many instances[3,4] by freeing the lower segment from the trachea, closing the tracheal opening, and anastomosing the upper and lower esophageal segments. In about one-half of the cases in which operation is successful, a postsurgical stricture forms and requires some form of dilatation. This will be noted by symptoms of dysphagia when a follow-up roentgenogram is made with barium three to four weeks after operation, or any time thereafter. Dilatation can frequently be initiated by using only the soft rubber, mercury-filled bougies in gradually increasing sizes. The subsequent management will be similar to the care of the congenital stricture.

A second and much less common type of atresia occurs in which both the upper and lower segments end blindly and neither can be sufficiently freed to allow anastomosis (figure 7). A gastrostomy will be necessary for nutrition, and the upper segment is brought to the skin surface above the clavicle on the left side to prevent constant spilling of saliva into

FIGURE 7. Congenital atresia of esophagus without esophageal fistula. The catheter has been passed into the blind lower segment of the esophagus through the gastrostomy opening.

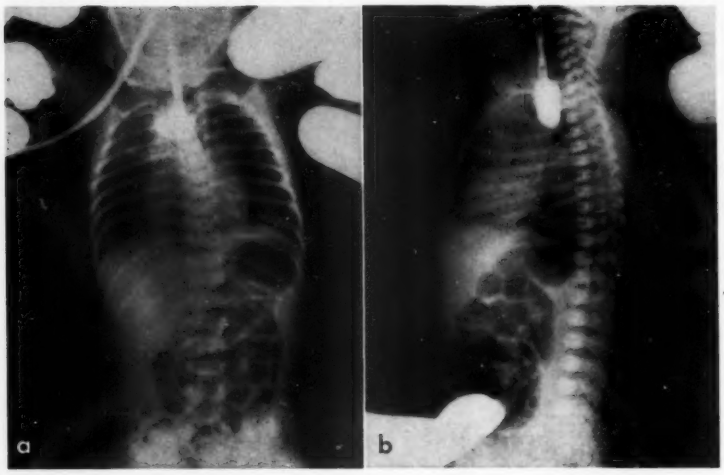

FIGURE 8a and b. Congenital atresia of esophagus and tracheo-esophageal fistula. A soft rubber catheter has been introduced into the blind upper segment. The air in the stomach and intestine indicates the presence of a fistula between the trachea and lower esophageal segment.

the larynx and trachea. Later, two years or more, a segment of bowel may be brought from below to accomplish an anastomosis with the upper segment.

Esophageal atresia in newborn infants will be recognized by the frothy saliva around the lips and the choking, coughing and regurgitation which follow attempts at swallowing feedings. If the presence of the abnormality is suspected, an esophagram is made, preferably by passing a small catheter into the esophagus through the nose or mouth and instilling 1 cc. of LIPIODOL® through the tube (figure 8). The blind upper segment will be visualized immediately. The roentgenogram, which includes the chest and abdomen, will frequently show scattered mottling in the lung fields or even an area of consolidation, com-

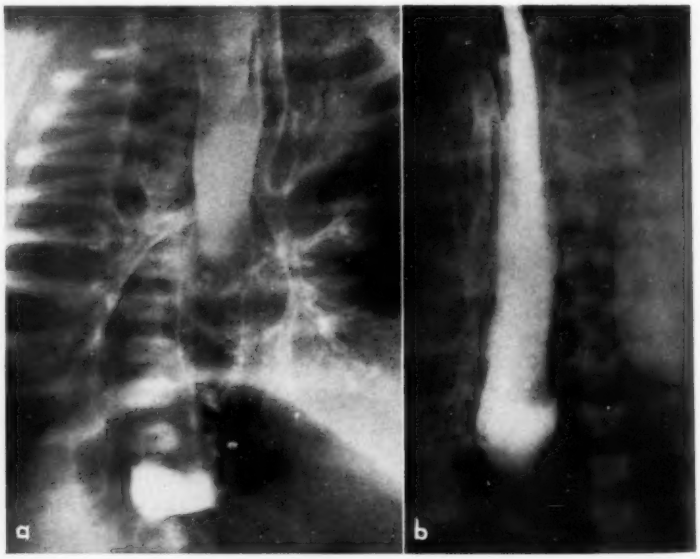

FIGURE 9a. Tracheo-esophageal fistula without esophageal atresia. b. Fistula demonstrated by the use of Lipiodol.

monly in the right upper lobe. If air is seen in the stomach or bowel, it indicates a connection between the lower segment and the trachea. The operation for correction of the lesion should be performed in the first four to five days of life. The best results will be obtained if early operation is done in cases in which there are no pulmonary complications. The operation preferably should be done after the child's weight exceeds 5 lb. When the roentgenogram shows no air below the diaphragm, the condition is an atresia without a tracheo-esophageal fistula. Surgical intervention then consists of performing a gastrostomy for nutrition and an esophagostomy on the upper segment as previously mentioned.

Esophageal atresia may be encountered with or without a tracheo-esophageal fistula, and, conversely, a tracheo-esophageal fistula may be present without esophageal atresia (figure 9). The latter condition may be difficult to diagnose. Occasionally, newborn infants will be found to have coughing and choking at each feeding, but a catheter can be passed into the stomach through the esophagus without difficulty. In the majority of these infants, the condition is probably neurogenic; the swallowing reflex is delayed and the condition ultimately rights itself. A persistence of symptoms would indicate a possible tracheo-esophageal fistula, and careful esophagoscopic, bronchoscopic and roentgenographic examination should be made to determine whether or not the symptoms are due to a spill-over from the pharynx or to a direct connection from the esophagus into the trachea. When a fistula is found, surgical closure is required.

Foreign Bodies

The presence of an esophageal foreign body should be suspected in an infant or child if a previously well youngster suddenly has a severe spasm of choking, coughing and gagging followed by dysphagia, salivation or regurgitation. A second person, possibly a member of the family, may have been present at the time and can name the object swallowed. The diagnosis in this instance is not difficult, and the subsequent steps in management will usually be obvious.

Occasionally, the choking episode alone will be observed, and the cause of the choking will then be obscure. There may be no immediate sequelae, and the usual tendency is to pass off the incident lightly, thinking it has no significance. Several hours, weeks or even months later, dysphagia or dyspnea or both may develop when esophageal and para-esophageal swelling has occurred, and a roentgenogram will reveal the presence of a foreign body in the esophagus.

To prevent such a sequence of events, a careful review of the situation should be made at the time of the choking episode. Consideration must be given to the toys being played with, and the accessibility of coins, safety pins and similar objects. If some portion of a toy or an object which was known to be at hand cannot be located, it should be assumed to have been swallowed.

It is, therefore, reasonable to state that if an infant or child has had an alarming choking spell and the parents are sufficiently concerned to have a physician see the youngster on this account, careful consideration should be given to the incident, and a fluoroscopic or roentgenographic examination of the chest and neck is indicated. If no direct or indirect findings are noted, and even if the child is having no symptoms of esophageal obstruction, an esophagram may be required for safety. In any case, subsequent close observation is indicated until all possibility of further trouble has passed. If, however, in spite of the lack of definite knowledge that an object has been swallowed, and with a negative roentgenogram, the child shows evidence of difficulty or discomfort on swallowing, esophagoscopy is indicated.

Roentgenographic study in the case of a suspected foreign body should consist of anteroposterior and lateral roentgenograms of the chest and abdomen, including the neck. On the lateral roentgenogram, the chin should be thrust forward and the arms held firmly downward and backward to present the cervical portion of the esophagus in a clear silhouette. If these roentgenograms show no evidence of a foreign body, an esophagram may be necessary. Visualization of the swallowing is ob-

tained fluoroscopically; spot films are made at whatever phase of the swallowing the foreign body would be most clearly outlined. If immediate esophagoscopy is anticipated, Lipiodol or IODOCHLOROL® should be used to avoid coating the mucosa and foreign body with white paste that makes direct visualization so difficult; otherwise, barium is preferable.

Successful esophagoscopic removal of foreign bodies in infants and children depends to a large extent on the proper choice of instruments. The use of a large esophagoscope will allow good visualization, but in an infant or a small child a large tube may rupture the esophagus and at least will seriously obstruct respiration and thus greatly limit the time of the procedure. The forceps must be adaptable to the necessary grasping and manipulation of the particular foreign body, and should be of proportionate diameter and length to allow adequate visualization through the esophagoscope employed.

A team of experienced assistants will expedite the procedure, and in most instances no anesthesia will be necessary. In cases in which the child is more than two years old, premedication with LUMINAL® sodium and morphine sulfate, or DEMEROL® and PHENERGAN® in proportionate doses will allow sufficient depression to permit a reasonably quiet procedure. Overdosage with these drugs may cause a marked depression and result in a sudden cessation of respiration during the esophagoscopic procedure.

Inhalation anesthesia may be necessary in some instances to obtain increased relaxation and when adequate assistance is not available. Ether is preferred in most cases. It is administered with an endotracheal tube to insure adequate ventilation while the esophagoscope is in place.

For the removal of pointed objects, notably safety pins, fluoroscopic visualization is of definite advantage. A proper grasp of the foreign body will often be best ascertained by this method, and the position and course of the object can be observed. A biplane fluoroscope is preferred, although the lateral beam is not often used for esophageal foreign bodies. A disk-shaped object, long retained in the esophagus, may be covered by granulation tissue, and will then be invisible endoscopically. In such an instance, the exact site can be noted, and the position of application of forceps will be directed by fluoroscopic guidance.

The most frequent esophageal foreign bodies found in children are disks, including coins, buttons, washers, etc. They are found in children usually between the ages of one and three years. The disk generally lodges in the upper part of the esophagus, either in the cervical portion or the area of the aortic narrowing, most frequently the former. The anteroposterior roentgenogram of the chest including the neck reveals the circular density at the clavicular level or just above it. The lateral roentgenogram shows the edge of the disk, and not uncommonly two or more coins are seen lying side to side.

Less frequently, a disk foreign body may pass the upper two constrictions and will be held at the cardia. It is not unusual for a coin to be suspended at the cardia for a short time and then pass spontaneously into the stomach. It is advisable to plan esophagoscopic removal in such an instance, but a fluoroscopic check should be made immediately before the procedure to make sure that the foreign body has not passed into the stomach. When the foreign body lodges in or near the midthoracic portion of the esophagus, it is well to examine this area carefully, either esophagoscopically or with an esophagram following the removal of the object, to determine whether or not a stricture has contributed to the obstruction.[1]

When safety pins are mentioned as foreign bodies, the open pin is implied. If it is closed, the pin passes easily through the esophagus and on through the gastrointestinal tract. Unfortunately, it seems always to be the open safety pin which is carelessly left within the baby's reach, or within range of the toddler's travels. Most children who swallow open safety pins are of the diaper age, that is, between six months and two years old. The child picks up the pin and, as a natural sequence, attempts to swallow it. Open safety pins are swallowed less frequently by infants who are less than six months old. In infants of this age, the accident is often due to an older brother or sister

who drops the pin into the baby's open mouth as he is crying in his crib.

Whether the history indicates that a pin has been swallowed or the parents merely suspect the possibility, either fluoroscopy or a full-length roentgenogram is advisable, first to determine the presence of a pin, and second to show its exact location. The roentgenogram should include the neck, since a large open pin most frequently will be found in the hypopharynx, point up, with the spring extending into the cricopharyngeal area. If the pin has passed through this region, it may lodge at any point along the length of the esophagus. In most instances, the point will be uppermost, the spring directed downward. The very small pins can be rotated in the esophagus and extracted with the point trailing. The medium-sized and large pins have to be carried into the stomach to accomplish rotation, or have to be straightened and removed with a trailing point.

An open pin which has passed freely into the stomach can be expected to pass spontaneously through the remainder of the intestinal tract. Each stool must be carefully examined, and, if the pin has not passed in three to four days, a recheck roentgenogram should be made to determine the progress of the foreign body. If it continues to move freely in the stomach or is advancing along the intestinal tract, no endoscopic or surgical interference will be necessary.

In those rare instances in which the safety pin is extremely large, or if it seems to be fixed in the stomach, and if it is made of a suitable metal, endoscopic removal under biplane fluoroscopy may be accomplished by using a magnet-tipped rod or a magnet on a string. When contact is made, the pin is brought into the lower part of the esophagus whence it can be removed perorally either with continued contact with the magnet or with rotation forceps.

Chemical Burns

Approximately two-thirds of the chemical burns of the esophagus occur in children under 10 years of age, and in 90 per cent of this group the children are less than five years old.[5] The accident occurs most often as a result of carelessness in leaving a caustic or corrosive solution in a container ordinarily used for a drinking cup or in a bottle within the toddler's reach. In the newborn and in infants, mistaken identity of drugs in the medicine cabinet accounts for a significant number of the accidents, when solutions such as LYSOL®, carbolic acid or lactic acid are used from bottles thought to contain cough medicine or cod liver oil.

The proportion of the chemicals encountered as causative factors of esophageal burns varies in different communities. Lye and its commercial derivatives are usually the principal offenders. Liquid ammonia is a frequent cause, followed closely by the corrosive acids.

The severity of the burn depends on the concentration of the chemical and the amount that has been swallowed. Caustic crystals will cause severe burns of the mouth and pharynx, and may result in severe burns of the esophageal mucosa. The condition of the buccal mucosa does not always reflect the state of the esophagus. It must also be remembered that a very small erosion of the esophageal mucosa, especially in the natural narrow portions of the lumen, can later cause a severe stricture. It is advisable to assume that an infant or child who has taken by mouth any amount of a potentially dangerous caustic or corrosive has sustained some damage to the esophageal mucosa. It is much safer to treat the youngster expectantly to avoid a stricture than to wait until a stricture develops.

During the first 24 hours after the accident, only liquids are allowed by mouth. Olive oil, 1 to 2 drams, is administered every three hours, and aspirin or sodium salicylate is prescribed as necessary for the relief of discomfort. If the burn is severe, it is advisable to order antibiotic coverage for at least a week. The place of cortisone therapy in the treatment of chemical burns of the esophagus has not yet been definitely determined. With the necessary lack of controls, the studies on this phase of treatment are equivocal, and a satisfactory result can be obtained in essentially all cases without the use of steroids. It is mandatory to use antibiotics in every case in which

cortisone therapy is instituted. Emergency treatment does not necessarily include the swallowing of a string, although this occasionally may prove of value for later dilatation in cases of extremely severe burns. Immediate gastric lavage will be indicated in cases in which a large amount of solution has been swallowed, since absorption of the poison would constitute a danger from a general standpoint. The esophageal trauma will not be lessened by passage of a gastric tube or by induced vomiting.

Daily dilatation of the esophagus should be instituted from 24 to 36 hours after the accident. The Hurst-type soft rubber, mercury-filled bougies are used, beginning with numbers 20 to 24 F. Two or three bougies, in increasing size, are put through the esophagus at each dilatation with the patient in the upright position and by allowing the bougie to descend into the stomach largely by its own weight. Each day, larger sizes are substituted, and by the end of the first week the numbers 32, 34 or 36 F. bougies will be passing easily. The ultimate size of the dilator will depend on the age and size of the child. If no resistance is encountered in the dilatation, the interval is increased to two or three times weekly, then once weekly, once in two weeks, and once monthly until approximately six months after the accident. At this point in the management, it is advisable to make a fluoroscopic and roentgenographic study with barium. If no evidence of stricture is seen, the prognosis is excellent, but dilatation at intervals of two to four months should be continued during the subsequent one and one-half to two years. The dilatations will serve as both therapeutic and diagnostic procedures, giving an indication of the formation of a stricture if this tends to occur. If the barium study shows evidence of a stricture, the dilatation will have to be continued at more frequent intervals, and close observation will be required.

In some instances, the patient is not seen until two to three weeks following the accident. It may still be possible to dilate the stenoses which have formed with soft rubber bougies, but the attempt should be made cautiously and no force should be used to pass the dilator through these areas. A satisfactory passage of the mercury-filled bougies will open the way for subsequent similar treatment. The dilatation should be repeated at necessary intervals to maintain and, if possible, increase the esophageal lumen. Esophagoscopy after early stricture formation is also extremely hazardous, and perforation is more likely to occur when this diagnostic procedure is used than immediately after the burn has occurred.

Occasionally, in cases of severe multiple strictures in which gross delay has occurred, all attempts at conservative management will fail. Consideration must then be given to surgical intervention to allow bypass of the obstructed esophagus.

Cardiospasm

Cardiospasm is relatively uncommon in infants and children. In 2 or 3 per cent of the cases, the cardiospasm occurs in the first decade, and it may be seen in the newborn.[6] When first suspected, the condition is frequently confused with congenital benign fibrous stricture. The symptoms of dysphagia and regurgitation are similar. The differentiation lies in the dilatation of the esophagus as seen in the esophagram and the ease with which the esophagoscope and the dilators pass through the distal part of the esophagus. The principal factor in treatment is the dilatation of the distal part of the esophagus with the mercury-filled bougies at necessary intervals to maintain satisfactory swallowing function. Improvement in nutrition will frequently result in improvement in swallowing. Supplementary therapy includes adequate vitamin and protein content in the diet, administration of the belladonna derivatives, and a mild sedative. The prognosis in most instances is good, although observation should be continued with dilatation from time to time if the symptoms seem to recur.

Esophageal Varices

Esophageal varices are relatively infrequent in children in this country, although common in children in Central America and South America. Their presence must be suspected when unexplained hematemesis or melena oc-

curs. The varices do not cause symptoms of esophageal obstruction nor are they easily detected in the esophagram. On esophagoscopic examination, the dilated veins are recognized in the distal part of the esophagus by the soft bulging contours and the faint bluish tinge of the overlying mucosa.

Frequently, the hemorrhage from esophageal varices will be massive at onset and will subside spontaneously without requiring any immediate therapy other than restoration of the blood lost. If bleeding continues, esophagoscopy may be done to determine the source and extent of the hemorrhage. The insertion of an OXYCEL® or GELFOAM® pack into the distal part of the esophagus through the esophagoscope may be necessary to control the bleeding.[7] In infants and children, the varices are often the result of portal vein stenosis or obstruction which produces clinical signs of Banti's syndrome. The best surgical curative procedure is therefore a portacaval shunt; if this is not possible, the second choice is a splenorenal shunt. Esophagoscopic injection of esophageal varices may be necessary to aid in controlling repeated hemorrhage in preparation for surgical intervention, or after surgical reconstruction has failed.

Esophagitis

Acute esophagitis is a frequent disease in infants and children. It may occur as an associated condition in cases of infectious fevers and as a complication of other esophageal diseases with intrinsic obstruction or with a foreign body. Inflammatory changes are found in the distal part of the esophagus of infants as a result of reflux of gastric juice, from either congenital dysfunction of the esophagogastric junction or persistent vomiting. The symptoms are due to esophageal spasm which may be reflected in the esophagram as a constriction of varying length, and will be noted esophagoscopically in the abnormal redness of the mucosa. Superficial ulceration may be seen, and the tissues bleed easily on contact with the instruments.

Treatment is directed primarily toward the underlying cause. The diet must be confined to soft bland foods. AMPHOJEL® or GELUSIL® and an inert powder, e.g., bismuth carbonate or bismuth subnitrate, are indicated. Belladonna derivatives may also be of benefit in controlling the muscular spasm.

Conclusion

The presence of organic disease of the esophagus must be suspected in infants and children with persistent dysphagia or regurgitation or those considered to be "feeding problems." With proper technics, an esophagram will, in most instances, afford sufficient evidence and indicate the nature of the disease. An anteroposterior chest roentgenogram and a lateral chest roentgenogram including the neck should be a routine part of the roentgenologic study. Barium is the medium of choice in esophagraphy, but Lipiodol or Iodochlorol should be used if a possibility of choking or aspiration of the contrast material exists.

Esophagoscopy is indicated to confirm the findings and to determine more exactly the true nature of the condition or to supply information which might not be obtained accurately by contrast study alone.

With the accurate methods of diagnosis which are now at hand and with the facility which attends endoscopic and surgical treatment, no physician should be content to develop an "await and see attitude" with an infant or child suspected of having esophageal dysfunction.

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The program of radiotherapy in treating malignant tumors of female reproductive organs should be planned as a unit, considering administration of radium, x-ray, telecobalt, etc. Not only must the gynecologist understand the nature and action of radiation, but also the radiotherapist must have a thorough knowledge of the female organs. Careful examination must precede initiation of radiotherapy. The author presents a discussion of irradiation in various gynecologic diseases based on experience at the Radiumhemmet, Stockholm.

The Role of Radiotherapy in Gynecology

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A FEW years after the discoveries by Röntgen and by Pierre and Marie Curie, roentgen and gamma radiation was tried in the treatment of carcinoma of the cervix and dysfunctional uterine hemorrhage. Radiotherapy soon proved to be of great significance in gynecology, and, since, it has assumed an important role in the treatment of gynecologic disorders.

H. L. KOTTMEIER

General Principles in Use of Radiotherapy

The proper use of radiotherapy requires great experience. It is not just a matter of putting a certain amount of radium into a tumor or of operating a machine to administer some thousands of roentgens to the parametrium. Not only must the gynecologist have a clear understanding of the nature and action of the radiation, but also the radiotherapist must have a thorough knowledge of the anatomy, physiology and pathology of the organs of the female pelvis. It should be emphasized that there is no exception to this rule. In general, it is not difficult to insert intra-uterine and intravaginal radium applicators under general anesthesia; nevertheless, the application of radium should not be considered separately from the administration of x-rays, telecobalt, etc. The program of radiotherapy should be planned as a unit. The application of the radium sources should be individualized in relation to the anatomic and pathologic nature of the particular case.

Radiotherapy is used in the treatment of malignant tumors to eradicate the growth while preserving the integrity of the normal tissue. In that respect, the tumor bed, i.e., the reaction of the host to the growth, has to be considered. Experience has shown that in the irradiation of a malignant growth the host relationship is as important as the direct effect of the ionizing rays on the cells. The frequent radiation injuries occurring at some institutions are attributable to improper administration of radiation, and, often, they cor-

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respond with the poor results obtained.

The biologic concept of the irradiation of malignant tumors of the female reproductive organs is that tumor cells, with their great mitotic activity, are generally more susceptible to damage than is normal tissue and that normal tissue recovers from radiation more rapidly than does neoplastic tissue. However, the germinal cells are an exception; therefore, the preservation of ovarian function cannot, in general, be considered in administering radiotherapy in gynecology.

In planning appropriate treatment, it must be remembered that the small bowel, the sigmoid, the rectum and the urinary bladder have much less tolerance to ionizing rays than do the uterus and the vagina.

Although a large dose of radiation is necessary to destroy a carcinoma, the radiotherapist must consider several factors in such cases. A large area of tissue will not tolerate the same dose of irradiation as a small area of tissue. The externally growing part of a tumor which has a good blood supply and is rich in A cells does not require as large a dosage of radiation as does the central part of the growth. At least, this has been the experience at the Radiumhemmet in the treatment of carcinoma of the uterus and rectum. Thus, in a case of carcinoma of the cervix, we administer a dose of at least 20,000 r to the cervix but give considerably less to the lateral pelvic wall. In accordance with the law of inverse square, the radiation that reaches the pelvic wall from the radium applied to the uterus and the vagina amounts to one twenty-fifth or less of that present at a distance of 1 cm. from the radium sources in the midline of the pelvis. Consequently, additional radiation has to be given to the parametrium with roentgen rays or by some other means in order to administer a satisfactory dose to the pelvic wall. But this does not mean that we have to employ a dose of 5000 to 6000 r. We believe that there is no proof that such a dose is always necessary to control a carcinoma in the parametrium.

Before radiotherapy is initiated, there should be a careful examination, including cystoscopy, proctoscopy, study of vaginal and cervical smears, biopsy and curettage. A roentgenographic examination, such as urography, will sometimes give information that is valuable in planning treatment. The patient's general condition should be as satisfactory as possible. Blood transfusions, vitamins and a high protein diet are of value. The psychologic factors also should be considered. We believe that it is important to inform the patient in detail about her disease and the treatment planned.

An elderly patient or one who has cardiovascular disease or syphilis is more likely to have radiation injuries; therefore, a full dose of radiation should not be given to such a patient. This is also true for a patient who previously has had a gynecologic operation or who has a local pelvic inflammatory disease.

One of the primary concerns of any radiotherapist should be to make his patient comfortable during the course of treatment. If the patient grows tired during therapy or if anemia or diarrhea develops, the irradiation should be postponed for several days. For these reasons, we at the Radiumhemmet prefer to fractionate the radiotherapy in malignant tumors of the female pelvis and to let the patients rest between the different phases of the treatment. During the last war we sometimes were forced to concentrate the irradiation. The cure rate in those cases was poor.

Fractionated treatment is valuable also because it is impossible to follow absolutely definite rules for curative or palliative therapy; nor can one decide at the initial examination whether curative or palliative treatment should be the choice in a given case, particularly in advanced malignancies. Palliative therapy can be performed intelligently. Although the therapist's primary objective may be to control the patient's symptoms, he can, by careful clinical observation, study the response of the tumor to the therapy. If there is no evidence of alteration of symptoms or in the extent of the disease following palliative treatment, further therapy is not indicated. However, if there is a good response, as shown by marked reduction of the total tumor mass, further definite therapy directed toward attempted cure can be undertaken.

The discussion to follow on irradiation in

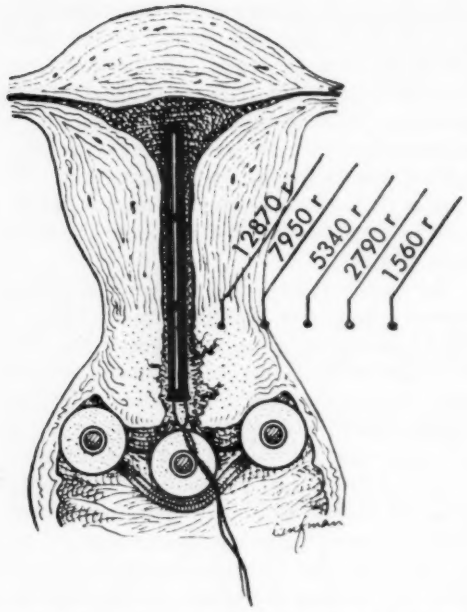


FIGURE 1. The Paris technic of distributing the radium dose in treating cancer of the uterine cervix.

gynecologic disease is based on the experience at the Radiumhemmet.

Cancer of the Uterine Cervix

Radiotherapy always should be the initial treatment for cancer of the uterine cervix. While many methods have been devised, generally, the combined use of radium and x-ray is recommended, with radium playing an important role. In that respect we fundamentally distinguish between the methods used.

The Paris method—This method is characterized by a protracted low-intensity technic. In a typical case, a rubber catheter containing 13.33 + 6.66 mg. or 13.33 + 13.33 + 6.66 mg. of radium is placed in the uterus, and a hard rubber colpostat containing 13.33 + 13.33 mg. or 13.33 + 6.66 + 13.33 mg. of radium is placed in the vagina for five to six days (figure 1). The Paris clinics recommend the intra-uterine and vaginal application of radium at intervals of a few days.

The Manchester method—This modification of the Paris method is intended to provide a predetermined physical dose to the paracervical triangle independent of applicator arrangements. The optimal dose is considered to be 8000 r. A schema has been drawn up which simplifies the use of radium and explains the popularity of the method; however, the various clinical types of the growth are not considered, which is a disadvantage.

Interstitial radium—In this method, needles are inserted into the margin of the cervix and into the parametrium from the vagina. Although good results have been reported, the number of injuries is high. At the Radiumhemmet, interstitial implantation of radium needles into the parametrium is sometimes done in addition to the typical treatment by radium.

The Stockholm method—Characterized by a fractionated high-intensity technic, this method employs various applicators. The filter is 2 to 3 mm. of lead. The intra-uterine applicators contain from 53 to 88 mg. of radium and are designed so that the dose rate is about 75 r per hour at a point 2 cm. from the midpoint of the applicator. The intravaginal applicators vary in size and shape, and, as a rule, deliver 60 to 80 mg. of radium. We intend to decrease the distance from the radium to the carcinoma and the pelvic wall as much as possible and simultaneously to increase the distance to the bladder and the rectum. For this reason, the radium applied to the vagina is spread out over a large area, and the rectum is carefully protected by gauze packing. For the same reason, the intra-uterine applicator is pushed up to the fundus of the corpus, and the lower 15 mm. of the uterine canal is not exposed to radium. This procedure also prevents subsequent pyometra. In uncomplicated cases the radium is left *in situ* for 27 to 30 hours. Three weeks later the radium application is repeated in essentially the same fashion. The total treatment period is determined from a direct reading of the dose in the posterior wall of the bladder and the anterior wall of the rectum. The optimal dose is 4000 γ r in the rectum and 5500 γ r in the bladder. As a rule, we do not exceed this dose in early stages of cervical carcinoma, but in advanced stages we give up to 6000 γ r in the rectum.

General principles—Clinical experience and the analysis of vaginal smears taken during the course of radiotherapy, as well as other observations, have convinced us that it usually is advisable to start radiotherapy in carcinoma of the cervix by applying radium, provided the external os is easily located and the vaginal growth permits a satisfactory application of the radium. Many factors other than these mentioned also must be considered. Thus, the dosage from the intra-uterine radium will be considerably increased, and that from the intravaginal radium will be decreased correspondingly (1) in endocervical carcinoma, (2) in case of spread of the carcinoma to the paracervical tissue in particular, (3) in the presence of metastases to pelvic lymph nodes, and (4) in a patient with a narrow vagina.

The dosage from the intra-uterine radium can be increased by prolonging the treatment time or by increasing the amount of radium to be applied. The latter method has been the more expedient. In order to avoid an overdosage to the uterine wall, the diameter of the intra-uterine applicator has been increased from 7 to 13 mm. Experience has shown that, as a rule, dilatation of the cervical canal to the diameter of a No. 13 Hegar dilator is easy in cases in which we want to increase the intrauterine dose. The position of the corpus in regard to the rectum also must be considered in choosing the proper applicator.

In all cases of carcinoma of the cervix, external irradiation from a 200 kv x-ray machine is given toward the parametrium and the pelvic lymph nodes through two anterior and two posterior portals. The roentgen therapy generally begins three weeks after the last radium application. A dose of 2000 to 2400 r is administered in an interval of 24 to 36 days. When the cancer has spread to the paravaginal tissue or has metastasized to the vaginal wall, 5 x 400 r of x-ray is also given from the perineal portals.

In cases of advanced parametrial spread of the carcinoma and of metastases to pelvic lymph nodes we give telecobalt through multiple small portals in addition to the irradiation described. We take advantage of the divergency of the cobalt beam and try to avoid overdosage to normal tissue. A careful examination of the pelvis, including urovenography, is required to accomplish such an irradiation. In this condition a total dose of 7000 gamma and roentgen units has been delivered to the pelvic wall.

In selected cases, vaginal injections of radioactive colloidal gold into the parametrium and lymph node-bearing tissue are of value. We do not use this method routinely at the Radiumhemmet, as experience has shown that late severe fibrosis may occur as a sequela of the administration of the isotope.

From 1949 to 1951, 1,092 patients with carcinoma of the cervix were referred to the Radiumhemmet for treatment. The five year cure rate is 89.0 per cent in stage I, 64.4 per cent in stage IIA, 45.2 per cent in stage IIB, 33.5 per cent in stage III, and 7.8 per cent in stage IV. The absolute cure rate is 50.5 per cent. Injuries to the bladder or rectum have occurred in 1.1 per cent of the cases and fistulas in 0.3 per cent. Except in the presence of metastases to the vagina, reirradiation of carcinoma which is recurrent or cannot be cured by radiotherapy is generally indicated only from a palliative viewpoint, provided a full course of radiotherapy has been administered initially. Otherwise, surgical intervention may be the treatment of choice, i.e., radical hysterectomy, exenteration or extensive fulguration.

Carcinoma of the Endometrium

A careful diagnosis is necessary before starting any kind of therapy. By fractionated curettage and histologic examination of specimens taken separately from the cervix and the corpus, it is generally possible to determine whether or not the endocervix has been invaded by a cancer. The degree of the histologic differentiation also should be considered. A highly differentiated adenocarcinoma does not tend to invade the myometrium as deeply as does an anaplastic carcinoma.

A panhysterectomy is indicated in a case of a well-differentiated adenocarcinoma limited to the corpus. Postoperative irradiation is advisable, and vaginal application of radium is important in order to prevent metastases. We

give 3000 γ r 1 cm. below the surface of the vagina (figure 2).

Primary radiotherapy is the treatment of choice in cases of anaplastic carcinoma of the corpus, in cases involving extension of the cancer to the isthmus or cervix, and for patients who are poor surgical risks. Many technics have been suggested. The Heyman packing method has led to good results. I like to stress the importance of ballooning out the uterine cavity by careful application of irradiators to the fundus. A uterine wall invaded by a malignant growth is relatively distensible. By using a careful technic, there is little risk of perforation or other complications. Thus, it is possible to decrease the distance from the radium to the cancer and to deliver a large dose to the growth. We divide the irradiation into two or three doses administered over a period of three to five weeks. A dose of 4000 to 5000 γ r is given to the anterior wall of the rectum. In advanced cases, however, it is advisable to shrink the uterus before inserting the radium; an intra-uterine tandem is helpful for this. The dose from the tandem is not considered in later treatment; 3000 mg. hours is given. In every instance radium is applied to the vagina.

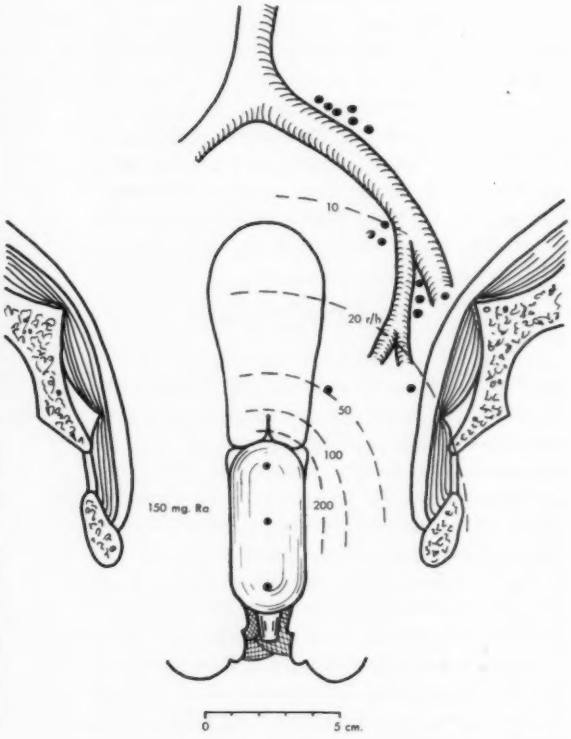


FIGURE 2. Intravaginal radium treatment of carcinoma of the uterus.

If the cervix is involved, additional irradiation will be given, as in cases of carcinoma of the cervix. Moreover, x-ray is given in advanced cases of carcinoma of the corpus.

Table 1 shows the results obtained in all cases of carcinoma of the endometrium treated at the Radiumhemmet over a 15 year period. The cases are divided according to the international classification and are selected; since many cases of corpus carcinoma considered good operative risks are operated on, they are not included in this table which gives the results of irradiation in cases of carcinoma of the endometrium.

Carcinoma of the Ovary

Although surgery is important in the treatment of ovarian cancer, the results achieved are very poor. Recurrences may appear anywhere and are common in the small pelvis. For this reason, the Radiumhemmet has stressed the significance of leaving the uterus for intra-uterine application of radium. A dose of 3000 γ r is given to the anterior wall of the rectum, emanating from 100 to 150 mg. of radium. In addition, the entire peritoneal cavity is irradiated through two anterior and two posterior fields (figure 3). Thus, it is possible to give a cancerocidal dose to the small pelvis and a palliative dose to the rest of the peritoneal cavity. Experience has shown that, as a rule, the degree of radiosensitivity cannot be estimated from the microscopic structures of the growth. A pseudomucinous carcinoma, however, is radioresistant, and a papillary carcinoma is often radiosensitive. Sometimes, obvious improvement from irradiation is noticed in cases of inoperable carcinoma or in cases in which it is impossible to remove all malignant tissue by operation. Under such circumstances, the x-ray therapy is repeated in two months. This is also true in cases in which it is believed that all of the growth has been re-

TABLE 1

RESULTS OBTAINED IN SELECTED CASES OF CANCER OF THE ENDOMETRIUM TREATED AT THE RADIUMHEMMET FROM 1936 THROUGH 1951

SITE OF GROWTH	AGE OF PATIENTS	OPERABLE CASES*		INOPERABLE CASES		TOTAL CASES		DEATHS FROM INTERCURRENT DISEASE
		Number	*Five year cures*	*Number*	*Five year cures*	*Number*	*Five year cures*	
Corpus	<40	16	14	1	0	17	14	1
	40 to 49	149	131	8	4	157	135	4
	50 to 59	519	401	48	12	567	413	30
	60 to 69	426	257	71	18	497	275	58
	70 to 79	162	66	31	5	193	71	43
	>80	6	3	2	0	8	3	1
TOTAL		1278	872 (68.2%)	161	39 (24.2%)	1439	911 (63.3%)	137 (9.5%)
Corpus and endocervix		138	64 (46.4%)	152	34 (22.4%)	290	98 (33.8%)	5
Uterus and ovaries						131	42 (32.1%)	

*Clinically inoperable cases are included in the operable cases.

moved by surgery. Results have been much improved by combining surgery with the fractionated irradiation mentioned. Recurrences in the pelvis are not common.

The results are extremely poor in cases in which the carcinoma is fixed to the surrounding organs and can be removed only with difficulty. Recurrences appear quickly and irradiation is inefficient in such cases. Therefore, we suggest that the abdomen be closed and that irradiation be used as described previously, and that the laparotomy be repeated about 10 days following the last day of the x-ray treatment. At that time the edema in the tissue will help loosen the growth from the surrounding organs.

Insertion of 120 mc of radioactive colloidal gold into the peritoneal cavity or 80 mc of the isotope into the pleura sometimes has a palliative effect in patients who have ascites or fluid in the pleura. Such an injection into the peritoneal cavity seems to be valuable also if given immediately after a laparotomy. The patient must turn in bed. A scintillation counter makes it possible to study the distribution of the isotope in the body.

In far-advanced cases of ovarian carcinoma, a tentative irradiation with a few large doses (3 x 700 skin r) directed toward the entire peritoneal cavity sometimes has been of value as an initial step. Blood transfusions are required in the course of such an irradiation.

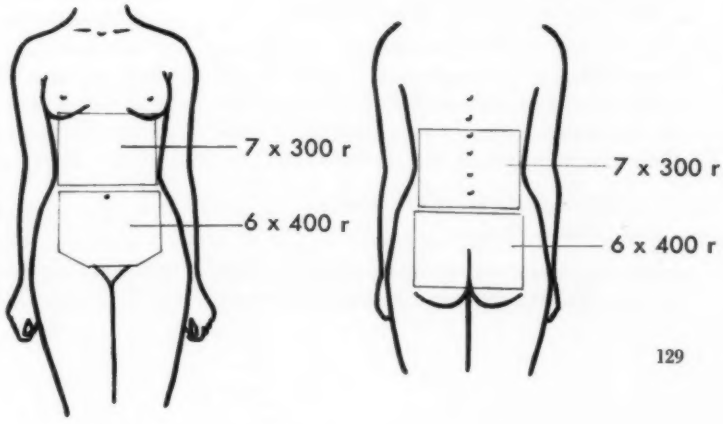
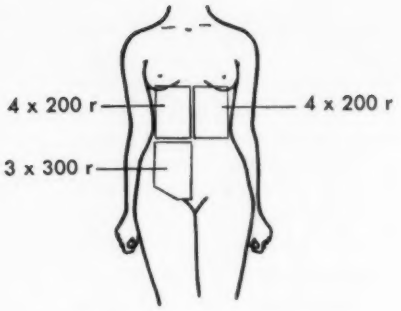


FIGURE 3. Anterior and posterior fields treated by x-ray in cancer of the ovary.



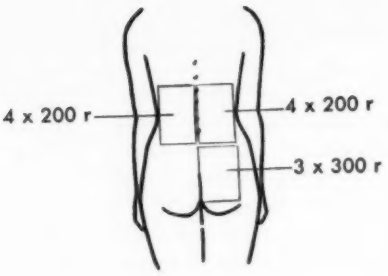


FIGURE 4. Anterior and posterior fields treated by x-ray in dysgerminoma.

Further therapy will depend on the reaction. Improvement has occurred in about 40 per cent of such cases seen at the Radiumhemmet.

Dysgerminoma of the Ovary

This type of tumor, which occurs in young women, is often unilateral. It metastasizes especially to the upper abdomen, the thorax and the supraclavicular glands. It is very radiosensitive. As a rule, small doses of x-ray therapy are given over several fields, but the normal ovary is not treated directly (figure 4). The irradiation may be repeated after some weeks. The results are satisfactory.

Granulosa Tumors of the Ovary

Tumors composed chiefly of sarcomatoid structures are malignant even if the pathologist cannot demonstrate malignancy by histologic examination. Granulosa tumors of the follicular or cylindroid type, as well as thecoma, do not need any irradiation if the total growth has been removed. The patients should have regular follow-up examinations for many years. Late recurrences do occur and often respond satisfactorily to irradiation.

Mesonephroma and Mesoblastoma

These rare tumors, occurring chiefly in young girls, are very malignant, and they generally are radioresistant. This holds true also for metastatic ovarian carcinomas, for instance, the Krukenberg tumors.

Dysfunctional Uterine Bleeding and Uterine Myoma

For many years x-ray sterilization therapy has been the treatment of choice in patients of preclimacteric and climacteric age who have abnormal uterine bleeding with or without uterine fibroids. An adequate dose of x-ray to the ovary is 350 r. At the Radiumhemmet we prefer an intra-uterine application of 64 mg. of radium for 16 hours. The results are excellent if the radium is applied in immediate connection with a careful curettage and if the uterus is smaller in size than a fist. The dose to the ovary does not exceed 150 γ r. X-ray sterilization therapy is confined to patients who are poor surgical risks.

Irradiation is contraindicated in patients less than 40 years of age who have functional uterine bleeding. X-ray therapy toward the spleen may be indicated in rare severe cases of blood dyscrasia.

Endometriosis

It is a well-known fact that x-ray sterilization therapy is used in cases of endometriosis in the urinary bladder or rectum and in endometriosis recurring after surgery. The results, however, are not always satisfactory. For years at the Radiumhemmet we have been administering small doses of x-ray directly to the endometriotic mass, combining this irradiation with the injection of testosterone propionate. As a rule, we do not exceed 200 r in a dose. Most patients obtain relief from their symptoms within a few weeks. Sometimes, repeated irradiation with small doses may be required. Many patients are not sterilized by this method.

Such a method of irradiation is sometimes of value also in severe cases of chronic pelvic inflammation, as in cases of tuberculous salpingitis with fistula in the bowels.

An orthopedic examination should be performed along with the routine physical examination, and history taking should include pertinent questions relating to orthopedic ailments. The author discusses the signs and symptoms which will lead to a cursory but adequate examination of the musculoskeletal system and points out the elementary principles which will prevent the physician's overlooking an orthopedic defect.

The Early Detection of Musculoskeletal Disorders

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ALL too often, the orthopedic aspects of the history and examination of a patient are overlooked, not investigated or considered unimportant. Such omission is due less to lack of interest on the part of the physician than to lack of instructional information concerning the basic questions, the significance of the replies, the details of the examination, and the interpretation of the physical findings. For example, patients may be treated for coronary disease when in reality the symptoms in the anterior part of the chest are due to extension of pain over the intercostal nerves from osteoarthritis of the thoracic segment of the spinal column, or they may be treated for pain in the abdomen when actually the symptoms are due to collapsed lumbar vertebrae, or they may be treated for thrombosis of the veins of the calf when, in truth, the symptoms are the result of rupture of the plantaris tendon.

The limited knowledge of the musculoskeletal system is noted especially in the hospital chart where the history and physical examination, as recorded by the house officer, indicate a definite inability not only to ask the proper questions but also to perform the simplest examinations. Rarely does one find a clear description of the orthopedic ailment. Although the hospital chart demonstrates that the well-trained house officer has mastered the use of the ophthalmoscope, the otoscope, the stethoscope, the uteroscope and the proctoscope, he does not understand the use of the goniometer. He can map out accurately, and takes the time to diagram, the neurologic deficit, but is lost completely in testing the muscle groups; he can identify and can recognize the significance of tenderness in the abdomen, but not in the lower part of the back; he understands the chest, but not the adjacent shoulder; he recognizes and charts the heart sounds, but cannot record the motion of the joints in degrees.

It is my intention, therefore, to review a few of the basic questions and basic signs which will lead to a cursory but adequate ex-

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amination of the musculoskeletal system, and to demonstrate that the examination of this system can be carried out with the regular examination, at the expense of only a few additional moments.

In taking the history pertaining to the different systems, the following questions will bring out any essential orthopedic ailment:

Are you troubled with any serious bodily disability or deformity?

Did you ever have a serious injury?

Was any part of your body ever paralyzed?

Did you ever break a bone?

Do you have numbness or tingling in any part of your body?

Are your joints often swollen and painful?

Do you usually have severe pain in the arms or the legs?

Have you had arthritis or rheumatism?

Do pains in the back make it hard for you to keep up with your work?

Do weak or painful feet make your life miserable?

Have you had any orthopedic or bone operation?

The orthopedic examination should not be set aside as a separate procedure, but should be performed along with the routine physical examination. As the physician examines one part of the body after another, the intervening musculoskeletal structures should be inspected. This can be done without prolonging excessively the time element. For example, at the time the neck is being palpated for lymphadenopathy and thyroid enlargement, motion of the neck should be tested in each plane. Limitation of rotation implies involvement of the first and second cervical vertebrae, while limitation of lateral bending implies involvement of the lower cervical vertebrae. The occurrence of pain in the arm at the extreme of any motion of the neck indicates disk disease; if tenderness occurs on one side of the neck and at the superior angle of the scapula, in association with pain in the posterior aspect of the upper part of the arm and hypesthesia in the fingers, rupture of a cervical disk must be considered. Pressure over the spinous processes localizes the individual vertebra that is involved; the affected fingers localize the involved nerve root and disk. If the diminished sensation involves the first and second fingers, the sixth nerve and the fifth intervertebral disk are involved; if sensation in the third finger is decreased, the seventh nerve and the sixth intervertebral disk are involved; and, if hypesthesia is present in the fourth and fifth fingers, the eighth nerve root and the seventh intervertebral disk are involved.

Passing from the neck to the shoulder, the examiner will detect the presence of subacromial bursitis by noting tenderness anteriorly with limitation of abduction and external rotation. Bursitis does not limit the muscle strength, and, therefore, can be distinguished from a tear of the supraspinatus tendon by the patient's ability to initiate abduction.

Below the shoulder, the presence of rupture of the biceps tendon can be determined by bunching of the muscle belly on active flexion of the elbow.

The most common affliction of the elbow joint is the so-called tennis elbow. Tenderness at the head of the radius suggests the presence of this condition. If flexing the wrist, pronating the forearm and extending the elbow cause pain which is referred to the elbow, the diagnosis of tennis elbow is confirmed.

In examining the wrist joint, one should not forget de Quervain's disease, which frequently is overlooked or mistaken for neuritis of the arm. If this disease is present, flexing the fingers over the thumb and adducting the wrist will produce severe pain which is localized to the styloid process of the radius.

In examining the back, it is not sufficient to lift the patient's shirt, thump his spinal column, and have him bend over. The patient should be in the standing position, and his back should be uncovered. The level of the pelvis and shoulders should be noted, because a deviation may be due to muscle spasm, curvature of the spinal column, or a short leg. One also should note whether the patient assumes a protective attitude or supports himself with one hand. Motion of the spinal column should be tested to demonstrate rigidity or mere limitation of motion at the extreme ranges. There is one cardinal sign of true low back pain which is present when few other

signs are evident; that is, the patient will designate the lower part of the back as the site of the pain when he bends backward or places the spinal column in extreme extension.

The posture should be observed while the patient still is standing. Round shoulders are one type of abnormal posture; the other is a sagging torso. The two types can be distinguished by having the patient assume the prone position. If the shoulders are rounded and the thoracic segment of the spinal column is rigid to firm palpation, the condition is due to wedging of the vertebrae and cannot be corrected by exercises, but, if the round shoulders become flat when the patient assumes the prone position and if the thoracic segment of the spinal column is flexible to firm palpation, the condition is due to ligamentous relaxation and should be treated by exercises.

While the patient is in the prone position, pressure should be placed on the spinous process of each vertebra from the neck down to the sacrum. This will reveal any area of tenderness, will localize the pain, and often will explain the roentgenographic appearance of the spinal column.

Tenderness immediately adjacent to the spinal column indicates muscle soreness due to spasm or injury. Particular attention should be given to pain localized in the lumbosacral joint, because this is overwhelmingly the most common site of low back pain. Tenderness on either side of the lumbosacral joint indicates strain of the ligaments, generally the iliolumbar ligaments. Tender nodules in the lumbosacral fascia (myogelosis) are due to herniation of fat. Although they are very tender, their excision seldom will cure the patient. Likewise, the presence of so-called trigger points is of no significance per se, and their presence is not diagnostic.

The sacro-iliac joints rarely, if ever, are the cause of pain in the back; in fact, they cause symptoms only in cases of tuberculous arthritis and arthritis of the Marie-Strümpell type. However, the tenderness frequently attributed to the sacro-iliac joint often is situated immediately below this joint, because it is here that the sciatic nerve leaves the pelvis by passing through the sacrosciatic notch. This point frequently is the first site of tenderness in cases of sciatica.

The sciatic nerves should be palpated for tenderness at the space between the tuberosities of the ischia and the medial borders of the greater trochanters of the femora, along their course in the posterior part of the thighs, and in the calves by squeezing the muscles to reproduce pain over the peroneal nerves.

It is necessary to distinguish backache due to the spinal column from backache due to renal disease. In the differential diagnosis of these two types of backache, the history is important. The original attack of acute orthopedic backache is due to injury, such as lifting. It may extend to the leg, and it often is severe enough to cause the patient to drop to the floor. Acute urologic backache usually does not occur after bending or lifting. It may extend to the abdomen, but it does not cause the patient to collapse suddenly. In cases in which the pain is chronic, the two types of backache are more difficult to distinguish, because easy fatigability, weakness and dull aching may be either urologic or orthopedic in origin. The following facts, however, should be kept in mind. Pain of renal origin is localized to the costovertebral angle. It may extend to the abdomen or to the groin, but it never extends to the leg. Low back pain is localized to the lumbosacral joint. It may extend to the leg, but never to the abdomen or to the groin.

In the course of the examination, the costovertebral angle should be palpated, and Murphy's test should be performed by striking the renal area with the closed fist. If this procedure elicits tenderness, it indicates that the pain is of renal origin. In fact, if tenderness is present at the costovertebral area but is not present in the spinal column, it is a definite indication that the pain is urologic in origin. If tenderness is present in the spinal column and also in the renal region, urologic consultation should be obtained.

Any tenderness of either sciatic nerve immediately rules out the kidneys as the cause of the backache. In cases in which the patients are elderly men, such tenderness suggests that disease of the prostate or rectum possibly might be the cause of the pain, since carci-

noma of either of these organs frequently causes sciatica. It is obvious, therefore, that a rectal examination is indicated in cases in which the patients are men. It also is indicated in cases in which the patients are women, because a calcified myoma of the uterus was found to be the cause of alleged backache in two cases which were observed recently. In both of these cases, the tumor was malignant.

While the patient is in the lying position, the leg signs should be elicited. Most of these signs are of questionable value, because they were designed to elicit pain in the sacro-iliac joints in the days when these joints were considered to be the cause of all backache. A few of these signs, however, are of value, and will be described because they are easy to elicit and are informative. In addition, they should be used in cases of suspected malingering, as well as in court cases, to obviate the opposing lawyer's asking, "What, you state that you performed a complete physical examination, but now you do not know whether Lasègue's sign is positive or negative?"

The best of the sciatic nerve signs is Lasègue's sign, which more commonly is known as the straight leg-raising sign. This sign is elicited by elevating the lower extremity while the knee is extended. If the knees can be extended to an angle of 90 degrees without causing pain, the sign is negative, but it must be remembered that short hamstring tendons will limit the motion of the leg. This sign is of value in demonstrating the presence of sciatica and muscle spasm of the lumbar segment of the vertebral column. It is of particular value in judging the results of treatment, because the sign gradually becomes negative as the patient improves.

Another sign which can be elicited easily and quickly is Ely's sign. This sign is elicited in the following manner. With the patient in the prone position, the leg is flexed on the thigh. If the patient elevates the pelvis on the same side to avoid pain, the sign is positive. This sign demonstrates the presence of sciatica and spasm of the lumbar muscles.

The best of the sacro-iliac signs is Gaenslen's sign. In eliciting this sign, the patient is placed in the supine position and drawn to the edge of the table. The lower extremity, which is on the table, is flexed onto the abdomen and held in position by the patient's hands about his knee. The physician then moves the opposite extremity downward into extension. The flexed extremity thus holds the ilium and sacrum in one position while the ilium on the opposite side is extended. This places tension on the sacro-iliac joint and will cause pain if the joint is affected.

Nachlas' sign is excellent in cases in which malingering is suspected. With the patient in the prone position, the back is extended by passively lifting both lower extremities. Then, without warning the patient, the legs are dropped onto the table. This will cause severe pain if true low back pain is present, but the patient will not complain if it is not present.

After the back has been examined, the motion of the hip joint should be tested while the patient is still supine. If both hip joints move equally without pain or spasm, a brief note to that effect should be written on the record. However, if motion should be limited on one side, the extent of motion should be recorded in degrees in relation to that on the normal side. Normal flexion of the thigh onto the abdomen is 45 degrees, complete extension is 180 degrees, abduction away from the midline is 45 degrees, adduction or crossing the thighs is 45 degrees, internal rotation is 35 degrees, and external rotation is 60 degrees. Limitation of these motions, with or without pain, indicates the presence of disease of the hip joint, and frequently is due to arthritis.

It should be remembered that pain in the hip often is referred to the knee joint, because the obturator nerve supplies both joints. Therefore, the hip joint should be examined if the patient complains of pain in the knee. Pain in the thigh also must be distinguished. Burning pain localized to the lateral half of the thigh and associated with hypesthesia extending from below the anterior superior spine of the ilium to above the knee is known as meralgia paraesthetica. It is a neuritis of the lateral femoral cutaneous nerve, not sciatica. On the other hand, pain along the posterior aspect of the thigh, which is generally deep and may extend into the calf, is due to sciatica.

As the patient sits on the edge of the table for examination of the reflexes, the knee joints should be flexed and extended with one hand, while the other hand is placed over the joint to determine fibrillation of the patella or crepitation of the joint. Digital pressure over the condyles or the joint lines will reveal tenderness due to an internal derangement of the knee. Holding the leg, in order to allow the patient to move the joint against resistance, will enable one to determine the muscle strength quickly. Normal motion is from a straight line at 180 degrees extension to 35 degrees flexion when the calf reaches the thigh. Any limitation on one side should be so recorded in degrees, such as 180 degrees to 35 degrees on the normal side while 160 degrees to 45 degrees on the abnormal side.

As the tibiae are being palpated for edema in the routine examination, the ankle joints should be inspected. Normal ankle motion is from 90 degrees dorsiflexion to 135 degrees plantar flexion. Tenderness or swelling can be palpated quickly, with particular reference to a small depression below the lateral malleolus, known as the sinus tarsi, which universally is the site of a sprain of the ankle, and tenderness in this area indicates such a condition.

After the dorsalis pedis and posterior tibial pulsations are palpated, the foot should be rotated to test the flexibility. The first toes should be examined for bunion formation known as hallux valgus, and for limitation of motion known as hallux rigidus. The latter condition is frequently mistaken for gout. The areas of tenderness in the foot are the heel, the apex of the longitudinal arch, and the heads of the metatarsal bones. Pain at the heel indicates a plantar spur or fascitis, pain at the apex of the arch indicates weakness or strain, and pain at the heads of the metatarsal bones indicates plantar warts, callosities or metatarsalgia. Plantar warts are distinguished from callosities by pressure and squeezing. Direct pressure on a callosity produces pain while squeezing does not, and, contrarily, squeezing of a plantar wart produces severe pain while direct pressure does not.

Pain localized to the third and fourth toes is due to a neuroma at the bifurcation of the digital nerves, and is commonly known as Morton's toe. Deep palpation between the heads of the third and fourth metatarsal bones produces marked tenderness. The correct diagnosis of this frequently overlooked condition will prevent the patient from using every conceivable orthopedic foot appliance and buying many pairs of shoes which are taken off every block or two with each attack of pain, and will make him deeply appreciative.

At the time the neurologic examination is performed on the lower extremities, it must be remembered that diminished sensation along the lateral aspects of the thigh, calf or foot, or along a narrow strip in the midline of the posterior part of the thigh and calf, and diminution or absence of the ankle jerk on the same side are pathognomonic of nerve pressure due to tumor or rupture of an intervertebral disk. However, one must remember that pain in the lower part of the back and the leg, even when made worse by coughing and sneezing, but without positive neurologic findings, is rarely if ever due to a ruptured disk. Almost universally, such findings are the result of inflammation and irritation of the nerve roots, due to a strain of the lumbosacral joint.

As the patient stands to dress, quick inspection will demonstrate whether or not the feet are flat, and, when he walks, inspection will reveal whether or not a limp is present.

Summary

An attempt has been made to demonstrate that an orthopedic examination can be integrated with a routine physical examination without inconveniencing the patient or adding more than a few minutes to the examiner's time. Moreover, a further effort has been made to point out the elementary orthopedic principles which will prevent the physician from overlooking an ordinary orthopedic condition. Obviously, the details set forth here are neither complete nor necessarily diagnostic within themselves, but they will at least prevent the nonobservance of an orthopedic defect, will indicate the parts which should be examined roentgenographically, and will allow the physician to plan a more detailed examination at a later date.

The clinical manifestations and the histopathologic picture of types of maculopapulosquamous dermatosis in children vary widely. Therapeutic results obtained from use of topical remedial agents also vary—from prompt response to stubborn resistance. The authors describe the more common types of dermatosis seen in children and suggest therapeutic regimens for each condition in which there is a known specific treatment.

Maculopapulosquamous Dermatosis in Children

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THE interesting skin diseases listed in table 1 are grouped together because of their similar clinical manifestations, i.e., macules, papules and scales. The last is indicated by the term squamous, from the Latin *squama*, meaning scale. Some of these diseases, such as tinea circinata and tinea versicolor, affect only the most superficial layer of the skin, the stratum corneum, in which the fungi lodge and multiply, and cause a mild inflammatory reaction. The salient features of such a superficial fungus infection include erythema, vesiculation and scaliness.

Pityriasis rosea, a skin disorder probably caused by a virus entering the body through the upper part of the respiratory tract, manifests itself dermatologically by lesions that may be macular, papular or vesicular, or maculopapular. Histologically, the picture is that of a nonspecific chronic dermatitis with changes in the upper part of the corium, in the rete malpighii and in the stratum corneum. Extreme degrees of edema in the epidermis may result in the formation of vesicles.

H. H. PERLMAN

A. B. FALK

Psoriasis, a disease known for its chronicity, manifests itself histopathologically in the stratum corneum (parakeratosis), in the epidermis (as Munro micro-abscesses), in a thinning of the suprapapillary areas of the rete malpighii, by elongation and clubbing of the rete pegs, and by dilatation of the superficial capillaries in the upper part of the corium. As one studies the clinical manifestations and the histopathologic picture of the types of der-

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TABLE 1

TYPES OF MACULOPAPULOSQUAMOUS DERMATOSIS

Psoriasis
Seborrheic dermatitis
Pityriasis rosea
Tinea circinata
Tinea versicolor
Parapsoriasis
Pityriasis rubra pilaris
Maculopapulosquamous syphilide
Lichen planus
Lichen nitidus
Lichen striatus

matosis in this group, he is impressed with the wide variations which they represent. Therapeutically, too, results vary from a prompt response to topical remedial agents (the fungus infections) to the most stubborn resistance to such therapy. Some of these dermatoses are self-limited (pityriasis rosea); others are characterized by involution that occurs spontaneously (lichen striatus and lichen nitidus); still others by remissions and recurrences (psoriasis). Because of the limitation of space, only some of the more common types of dermatosis will be discussed here. Tinea versicolor, pityriasis rubra pilaris and the maculopapular and squamous syphilides will not be considered.

Psoriasis

Psoriasis is seen infrequently in children under the age of five years. Essentially, the skin manifestations do not differ from those seen in the adult except that the guttate type is perhaps more common in early childhood. In typical cases, diagnosis is based on the symmetrical distribution of the lesions, plaques of hyperkeratotic micaceous scales located over the elbows and knees, on the trunk and throughout the scalp. The characteristic mother-of-pearl scale yielding bleeding points on its removal and the chronic course render the diagnosis comparatively simple.

The primary lesion is a pinpoint to pinhead-sized, or somewhat larger, round lesion, a slightly elevated macule or maculopapule of a reddish to reddish-yellow color, which disappears under pressure. Gradually, as the lesion grows older and enlarges, it becomes covered with silvery micaceous scales (figure 1a)

FIGURE 1a and b. Chronic psoriasis in an 11 year old boy. Note the erythematous scaly lesions on the lower extremities (a) and the piled-up (hyperkeratotic-parakeratotic) plaques with the micaceous scales on the upper extremities (b). Thickened scales also were present on the scalp and trunk. The dermatosis had been present since the boy was three years old. This boy was very much overweight. The basal metabolism was –34 per cent.

over the entire psoriatic patch although the border may be erythematous. When the piled-up scale (hyperkeratosis) (figures 1b and 2) is removed, a smooth papule remains.

The scalp is commonly involved in children, and there may be combinations of the guttate (figure 3) and nummular types over the trunk

FIGURE 2. Classical plaques in case of chronic psoriasis. Note the sharply demarcated, piled-up, mother-of-pearl plaques commonly observed in cases of this disease.

and the extremities. However, the generalized and universal type of psoriasis is seldom seen in children.

Psoriasis of the trunk and the extremities must be distinguished from seborrheic dermatitis, atopic dermatitis, papulosquamous syphilide, pityriasis rosea and lichen planus. Psoriasis of the face (rare) must be distinguished from lupus erythematosus. Psoriasis of the intertriginous areas must be distinguished from fungus infection (moniliasis). Psoriasis of the scalp must be distinguished from tinea capitis and seborrheic dermatitis.

Treatment—Dermatologists do not speak of a cure for psoriasis. Psychologically, it is important to explain the condition to the parents and to inform the older child that the active lesions can be kept under control by proper topical measures.

The indications in treatment are to remove the hyperkeratotic lesions and to attempt to prevent their recurrence by the use of appropriate topical agents (figure 4) as well as by certain modalities of treatment (Goeckermann treatment). The remedies employed topically are classed as keratolytics and reducing agents. Itching as a rule is slight in children, although it occurs frequently in adults (approximately 40 per cent of the patients). The intake of fats and fatty foods should be reduced to a minimum. Overwork at school or an extra-heavy schedule with its associated anticipation and worry, and late hours may precipitate a new attack. So, too, foci of infection, diseased tonsils, etc., may provoke the development of new lesions. High-strung and emotional children should obtain sufficient rest, both physical and mental, and adequate sleep.

The remedial topical agents employed in the management of psoriasis may be divided into four types: (1) salicylic acid, (2) the tars, (3) chrysarobin and derivatives of this chemical, and (4) the corticosteroids. These may be used as ointments, creams and, in some instances, as paints, alone or in various combinations.

The Goeckermann treatment utilizes tar as the topical agent. It is painted on the lesions

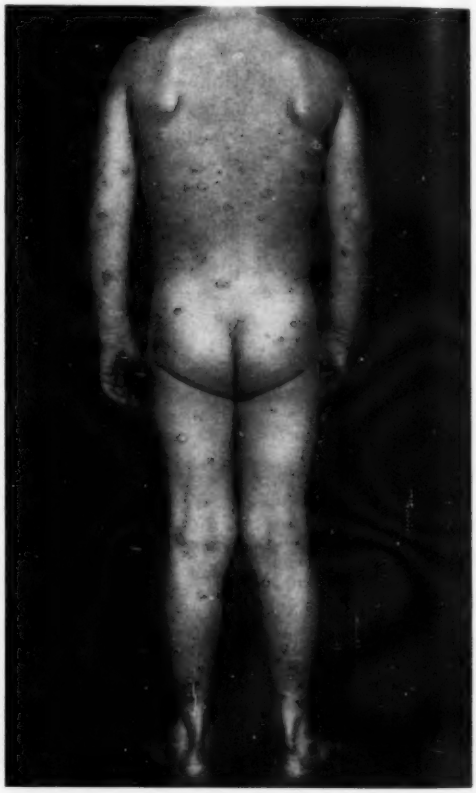


FIGURE 3. Guttate type of psoriasis in a young girl. The silver scales, some larger than a drop, are distributed generally over the trunk and the upper and lower extremities. The father of this girl and her paternal grandfather also had psoriasis.

FIGURE 4. Generalized psoriasis in a five year old boy. This boy shows the effect of topical application of an antipsoriatic ointment (5 gm. of salicylic acid, 5 gm. of ammoniated mercury, and a sufficient quantity of equal parts of zinc oxide ointment and 5 per cent pine tar in hydrophilic petrolatum to make 100 gm.). The ointment was applied nightly before bedtime, and its application was preceded by a bath with Fels-Naptha soap and water. Note the erythematous annular lesions, which were covered with piled-up micaceous scales before treatment. The lesions also were present on the scalp. The von Auspitz sign (bleeding points) was positive.

(liquor carbonis detergens), or, instead, a tar ointment is applied to the lesions and is followed by ultraviolet light from a mercury-vapor, air-cooled quartz lamp.

In applying remedial agents topically, it is important, first, to get rid of the hyperkeratotic scales by means of a warm bath with a strong alkaline soap, for example, Fels-Naptha soap or Octagon soap. A simple ointment base, e.g., petrolatum, containing 5 to 10 per cent of salicylic acid and an equal concentration of ammoniated mercury is then rubbed into the lesion. An ointment containing 0.1 to 0.25 per cent of ANTHRALIN®* also is useful. Although the corticosteroid ointments are useful topical agents in some cases, they have not been as effective as had been anticipated. Various combinations of these ointments with tars and antibiotics are now being marketed.

The following prescriptions represent the manner of ordering keratolytics and reducing agents.

PRESCRIPTION NO. 1

Ammoniated mercury (6 per cent)	6.0
Salicylic acid (6 per cent)	6.0
Hydrophilic petrolatum	
Rose water ointment (without rose oil) āā q.s. ad	100.0

Misce et fiat unguentum.
Signa: Apply by inunction before bedtime. Bandage parts.

PRESCRIPTION NO. 2

Pine tar ointment N.F.	
Zinc oxide ointment āā q.s. ad	100.0

Misce et fiat unguentum.
Signa: Apply before bedtime. Bandage parts.

PRESCRIPTION NO. 3

Salicylic acid (2 per cent)	2.0
Coal tar solution (5 per cent)	5.0
Ammoniated mercury (5 per cent)	5.0
Hydrophilic petrolatum q.s. ad	100.0

Misce et fiat unguentum.
Signa: Apply before bedtime. Bandage parts.

*Anthralin N.F. is 1,8,9-anthratriol (dihydroxy-anthranol). Ointments containing 0.1, 0.25, 0.5 and 1 per cent, respectively, of Anthralin are supplied by the Abbott Laboratories, Inc.

Seborrheic Dermatitis of the Glabrous Skin

Seborrheic dermatitis begins either as a papular folliculitis which enlarges to form a plaque or as a circinate or oval, yellowish or reddish-yellow, scaly lesion. The lesions are demarcated, or they may be covered by dry scales. They may be exudative and later crusted. Frequently the oval-shaped lesions following the lines of rib cleavage resemble the full-blown lesions of pityriasis rosea. Seborrheic dermatitis of the axillae (figure 5a and b) and the intercrural regions may closely simulate tinea cruris; at times, clinical differentiation

FIGURE 5a and b. Seborrheic dermatitis of the glabrous skin and scalp of a two month old infant. Note the sharply marginated plaque over the upper part of the thorax, the upper part of both arms, and the axillae. A similar eruption also was present on the scalp (cradle cap), behind the ears, and on the neck, eyebrows, each side of the nose, and the buttocks. Improvement followed the use of an ointment consisting of equal parts of Vioform cream (3 per cent) and rose water ointment (without rose oil).

is difficult. During warm, humid weather, the lesions may become eczematous as a result of rubbing or scratching.

Pruritus when present is usually mild. There are no constitutional symptoms. Seborrheic dermatitis of the glabrous skin must be distinguished from papular syphilide, psoriasis, pityriasis rosea and tinea cruris.

Treatment—Chemicals and pharmaceutical preparations employed in the treatment of seborrheic dermatitis are known as keratoplastics (skin softeners) or peeling (desquamating) agents (keratolytics). The object of the topical use of these agents is either to soften the scales and crusts or to peel them away. Furthermore, it is important to prevent secondary infection of the affected parts from scratching or rubbing, and finally to prevent a recurrence. There are many keratoplastic and keratolytic agents that can be employed. Examples are salicylic acid, precipitated sulfur, resorcinol, all the tars, ammoniated mercury and VIOFORM®.* All the fixed oils, e.g., olive oil, cottonseed oil and peanut oil, are in a sense skin softeners (keratoplastics), and many of the unctuous preparations such as goose grease, cold cream, benzoinated lard and the aliphatic hydrocarbons, liquid petrolatum, possess a keratoplastic property. If less than 3 per cent of salicylic acid is added to a simple ointment base such as rose water ointment, it is keratoplastic; on the other hand, if a higher percentage of salicylic acid is added, it is keratolytic. Since rose water ointment is alkaline, more than 3 per cent of salicylic acid never should be added to this ointment base. If more salicylic acid is added, it will "crack" the ointment and render it unfit for use.

The following prescriptions have been found useful in the treatment of seborrheic dermatitis.

*Vioform is a trade name of iodochlorhydroxyquin U.S.P. Vioform ointment (3 per cent) is supplied by Ciba Pharmaceutical Products, Inc.

PRESCRIPTION NO. 1

Salicylic acid (0.5 to 1 per cent)	0.5 to 1.0
Hydrophilic petrolatum	
Rose water ointment (without rose oil)	
āā q.s. ad	100.0

Misce et fiat unguentum.
Signa: Apply to lesion t.i.d.
Indication: Keratoplastic.

PRESCRIPTION NO. 2

Vioform ointment (3 per cent)	
Rose water ointment (without rose oil)	
āā q.s. ad	100.0

Misce et fiat unguentum.
Signa: Apply t.i.d.

PRESCRIPTION NO. 3

Salicylic acid (3 per cent)	3.0
Precipitated sulfur (3 per cent)	3.0
Hydrous wool fat	
Petrolatum āā q.s. ad	100.0

Misce et fiat unguentum.
Signa: Apply t.i.d.

FOSTEX® cream* has been found useful for the treatment of seborrheic dermatitis of the scalp and glabrous skin.

Pityriasis Rosea

The diagnosis of pityriasis rosea is based on the following clinical criteria:

1. The presence of a herald patch (figure 6), which also is known as a primitive patch, sentinel patch or mother lesion, and which is generally mistaken for ringworm. It is most often seen on the trunk, but it may appear anywhere on the body. The herald spot is not always found; indeed, it frequently is overlooked or is masked by the application of topical dressings. When found, it is round or oval. It usually precedes the generalized eruption seen on the trunk (figure 7) by one to four weeks (average, 10 days).

FIGURE 6. Pityriasis in a Negro girl. The "mother lesion" (herald patch) may be seen on the external genitalia, which have become eczematous.

(PERLMAN, H. H. and LUBOWE, I. I.: Pityriasis rosea in children. J. Pediat. 40:109 [January] 1952.)

*This preparation is supplied by Westwood Pharmaceuticals (Division of Foster-Milburn Company).

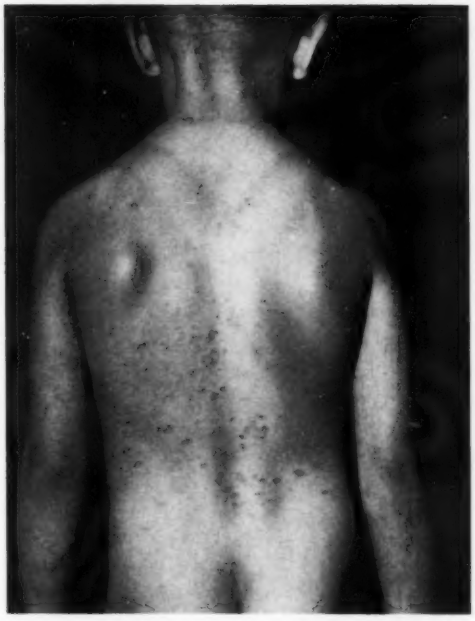


FIGURE 7. Pityriasis rosea (early lesions) in a boy. The oval-shaped pinkish scales are beginning to appear on the trunk 10 days after the "sentinel" lesion, which appeared over the precordial region.

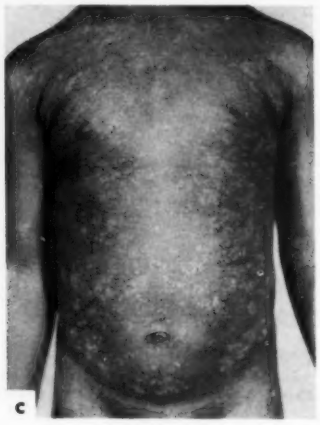
(Reproduced through the courtesy of Drs. Carroll S. Wright and Reuben Friedman.)

2. Mild prodromal symptoms of a cold, such as sore throat, malaise and nervous irritability. A generalized adenopathy may be present, and there may be a slight elevation of the temperature.

3. An eruption, which at first is macular (figure 8a, b and c), papular, maculopapular or even vesicular. It is, for the most part, distributed on the trunk. The scalp of children is frequently involved (figure 9), as is sometimes the mucous membrane of the mouth. The individual lesion appears to be salmon colored. It generally is oval shaped, and has a

FIGURE 8a, b and c. Pityriasis in a three year old Negro boy. The macular eruption, which is fully developed, is characterized by oval-shaped lesions. The scale resembles that of cigarette paper. At the height of their development, the lesions on the trunk have been compared to an inverted Christmas tree. The "scale" breaks, so that the center of the oval-shaped lesion remains free of scale, but the scale remains attached to the periphery of the lesion. Folliculitis is common in persons who have a dark skin.

(From PERLMAN, H. H.: Pediatric Dermatology. Chicago, The Year Book Publishers, Inc. In preparation.)



thin, crinkled scale like that of a cigarette paper. The center of the scale becomes loose while the periphery remains firmly attached. The free edges of the scale are directed toward the center. The center of the macular lesion may be completely or partially clear, fawn-colored, and surrounded by a rosy ring. The oval-shaped lesions tend to follow the cleavage lines of the ribs. When the rash is fully developed, it has the outline of an inverted Christmas tree.

The most important types of dermatosis with which pityriasis rosea may be confused include tinea circinata, macular syphilide, psoriasis, disseminated seborrheic dermatitis, lichen planus and scabies.

Treatment—Pityriasis rosea is a self-limited disease which runs its course in 6 to 10 weeks. Probably the most important consideration is *not* to overtreat this condition, for overtreatment unquestionably may prolong infection. All of the preparations prescribed for topical application should be soothing (antiphlogistic) and should make the patient comfortable. Pityriasis rosea does not recur as a rule, and it does not leave any sequelae.

The use of soap and water should be avoided. In their place, colloidal baths, such as AVEENO® colloidal oatmeal baths or starch baths, should be used.

There is no specific remedy for this disease, but certain modalities can shorten its duration. Of these, generalized exposures to ultraviolet light from an air-cooled mercury-vapor quartz lamp perhaps are the most useful. In using the quartz lamp, it is important to produce very slight erythema of the skin, for suberythema doses have little or no effect. The results of ultraviolet therapy probably are due to superficial exfoliative dermatitis.

One of us (Perlman) and Lubowe have obtained excellent results with foreign protein therapy. Typhoid-paratyphoid vaccine was given to older children. Two or three doses of 0.5 cc. were administered at intervals of five or six days. PROTEOLAC® also may be used.

FIGURE 9. Pityriasis on the face and scalp of a Negro boy. The scalp is commonly involved in children.

(PERLMAN, H. H. and LUDOWE, I. I.: Pityriasis rosea in children. J. Pediat. 40:109 [January] 1952.)

Leiner, a Viennese pediatrician, used injections of milk for their nonspecific effect. In cases in which these injections were used, desquamation began in four or five days, and involution began at the end of a week.

Burow's emulsion (Rosen's emulsion) has been found to be most useful. This emulsion contains aluminum acetate solution, and 0.125 or 0.25 per cent of menthol is added for its antipruritic effect. It is prepared in the following manner.

Lanolin	30.0
Olive oil	130.0
Heat in a mortar and mix very well.	
Add menthol (0.25 per cent)	0.75
Mix very well.	
Add zinc oxide and talc āā	30.0
Mix very well.	
Add aluminum acetate solution	6.0
Mix very well.	
Add calcium hydroxide solution q.s. ad	300.0
Mix very well.	

This emulsion should be dispensed in a wide-mouth bottle, and it should be applied to the lesions p.r.n. with a paint brush.

Tinea Circinata

Ringworm of the glabrous skin, a superficial fungous infection, causes lesions that are macular, papular, vesicular and scaly. The primary lesion is either a tiny red macule or a slightly raised papule. The lesions are usually found on the exposed areas of the body: the face, the neck or the upper extremities, although any part of the body may be affected. The most common form of ringworm of the glabrous skin is the macular or the dry type (figure 10).

The lesions are few in number, and there usually is but a single lesion. Seldom are there more than a half dozen. They appear as discrete, pinkish or reddish circinate lesions varying in size from that of a small pea to that of a quarter of a dollar or even larger. The ring-shaped lesions appear on a level with the rest of the skin or are only slightly raised above it. Some scaliness appears at the center. The lesions gradually enlarge by spreading peripherally, so that, within a week or two, circumscribed, circinate (coin-shaped) lesions are seen. The center of the lesion is paler than the periphery, and the scaliness is also greater in the peripheral area. Closer examination will show several reddened rings arranged concentrically within the outermost border. As a rule, the outermost margin of the

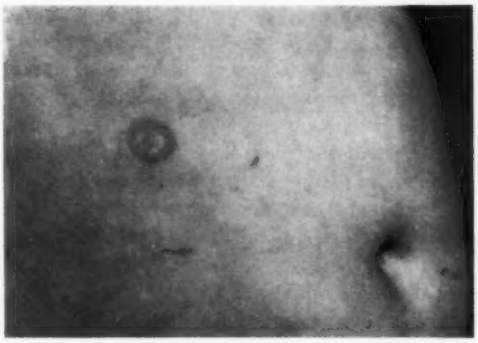


FIGURE 10. Tinea circinata (ringworm of the glabrous skin) in a five year old boy. Note the circinate, scaly lesion on the right side of the abdomen (duration, one week). The ringed lesion shows a tendency to clear in the center while spreading peripherally. The border of the lesion is raised and is studded with numerous small vesicles. Culture on Sabouraud's medium disclosed *Microsporum lanosum* (animal type). The lesion responded promptly to application of 3 per cent each of ammoniated mercury and salicylic acid in rose water ointment (without rose oil).

lesion is sharply defined, so that it appears as a raised border topped by a series of small vesicles.

Confirmatory evidence may be secured by scraping the lesion, applying a few drops of a 10 to 15 per cent solution of potassium hydroxide to the scales, and examining them for mycelian threads with the microscope. Culture on Sabouraud's medium will disclose the fungus.

Ringworm of the glabrous skin may be confused with atopic dermatitis, pityriasis rosea, circinate syphiloderm, psoriasis, seborrheic dermatitis, lupus erythematosus and granuloma annulare.

Treatment—In the treatment of ringworm of the glabrous skin, the objectives are: (1) to prevent the infection of other persons, (2) to produce healing in the shortest possible time, (3) to prevent complications caused by the trichophytid, and (4) to prevent a recurrence of the disease. Complications occur less frequently in cases of tinea circinata than they do in cases of tinea capitis.

It goes without saying that children with ringworm of the skin should not be permitted to attend school, to go to places of amusement, or to make contact with uninfected playmates until all evidence of active disease has disappeared. When ringworm is present in puppies (figure 11) and in kittens in a household, these animals themselves should receive active therapy for the infection or should under certain conditions be removed from the home. Ringworm of the glabrous skin, whether due to the human type *(Microsporum audouini)* or the animal type *(Microsporum lanosum)*, is amenable to the topical use of fungicidal and fungistatic remedies. Many of the remedial topical agents employed for the management of tinea circinata are keratolytics, and by their peeling effect on the stratum corneum carry away the fungi lodged in the superficial layer of the skin. Benzoic and salicylic acid ointment U.S.P. XV (Whitfield's ointment),* iodine, ammoniated mercury and precipitated sulfur, used alone or in various combinations, are useful as fungicides. The following prescriptions indicate how such remedies may be prescribed.

PRESCRIPTION NO. 1

Benzoic and salicylic acid ointment
Rose water ointment (without rose oil)
āā q.s. ad 30.0
Misce et fiat unguentum.
Signa: Apply to lesions several times a day.

PRESCRIPTION NO. 2

Iodine (3 per cent) 0.9
Goose grease or hydrous wool fat q.s. ad 30.0
Misce et fiat unguentum.
Signa: Apply to lesions several times a day.

PRESCRIPTION NO. 3

Compound undecylenic acid ointment N.F.† 30.0
Signa: Apply to lesions several times a day.

PRESCRIPTION NO. 4

Ammoniated mercury ointment
Petrolatum āā q.s. ad 30.0
Misce et fiat unguentum.
Signa: Apply to lesions several times a day.

PRESCRIPTION NO. 5

Tincture of iodine (2 per cent) 30.0
Signa: Apply to lesions with a cotton applicator twice a day.

Parapsoriasis

The characteristic features of parapsoriasis are (1) its chronicity and (2) its failure to respond to therapeutic agents. In three of the varieties, namely, parapsoriasis guttata (figure 12a and b), parapsoriasis lichenoides and parapsoriasis en plaques, the maculopapular lesions are capricious and persistent. Pityriasis lichenoides et varioliformis acuta, in contrast to the previous types, consists of vesicles, papules and papulonecrotic lesions which terminate in varioliform scars; hence, the name. This form of parapsoriasis, which runs an acute course, undergoes involution in from a few weeks to a few months. In the acute phase, this form of parapsoriasis may be confused with varicella.

Parapsoriasis should be distinguished from psoriasis, seborrheic dermatitis, lichen planus,

*Benzoic and salicylic acid ointment, U.S.P. XV, is not as strong as the similar preparation listed in N.F. IX. The composition of the U.S.P. preparation is as follows: benzoic acid 6.0, salicylic acid 3.0, and polyethylene glycol ointment 100.0.

†This ointment, N.F. X, contains undecylenic acid 5.0, zinc undecylenate 20.0 and polyethylene glycol ointment 100.0.

FIGURE 11. Tinea circinata on exposed areas of skin of mother and child. Disease was contracted from a stray dog. Culture disclosed *Microsporum lanosum*. In cases of tinea circinata, there seldom are more than six lesions.

(Reproduced through the courtesy of Drs. Carroll S. Wright and Reuben Friedman.)

papular syphilide, pityriasis rosea and from leukemia.

Pityriasis lichenoides et varioliformis acuta should be distinguished from varicella, atypical variola, papular or papulopustular syphilide, papulonecrotic tuberculide and atypical pityriasis rosea.

Treatment—There are no specific remedies. Some investigators have obtained good results with generalized exposure to ultraviolet light from an air-cooled mercury-vapor quartz light. One investigator has obtained unusually good results by using calciferol for parapsoriasis guttata and pityriasis lichenoides et varioliformis acuta.

Lichen Planus

Lichen planus is relatively uncommon in children. Diagnosis is comparatively simple because of the classic clinical picture characterized by angular shiny papules (figure 13) of a violaceous (lilac) color, many of which are umbilicated. The lesions usually appear on the flexures of the forearms, the legs, the inner aspects of the thighs and of the ankles, and also in the sacral area. White lines or puncta may be seen running over the papules, the so-called Wickham striae. Infants may have

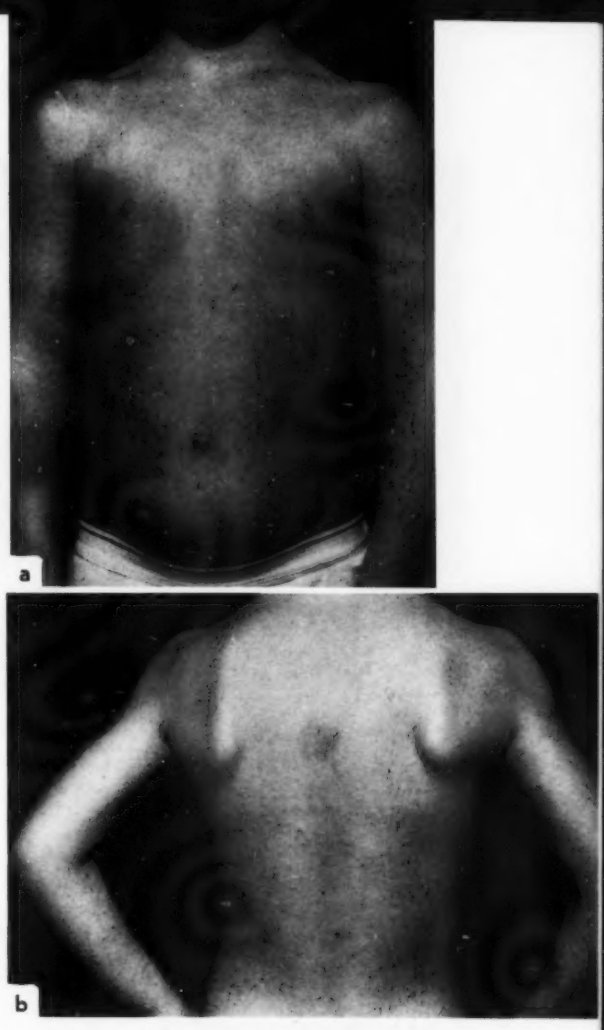


FIGURE 12a and b. Parapsoriasis (guttate type) in a seven year old boy. Lesions had been present for four months. Note the erythematous scaly lesions on the trunk and upper extremities. The thighs also were involved. There was no itching. This type of parapsoriasis not infrequently is mistaken for the guttate type of psoriasis, but these two types of dermatosis are not related. The histologic appearance of the lesions was compatible with that of parapsoriasis.

(From PERLMAN, H. H.: Pediatric Dermatology. Chicago, The Year Book Publishers, Inc. In preparation.)

papulopustular lesions associated with bullae. The oral mucous membranes may show a reticulated plaque. Itching is slight compared to pruritus in the adult.

Generalized lichen planus in infants and children should be distinguished from scabies, pediculosis corporis, pityriasis rosea, guttate psoriasis, lichenoid syphilide, lichen scrofu-

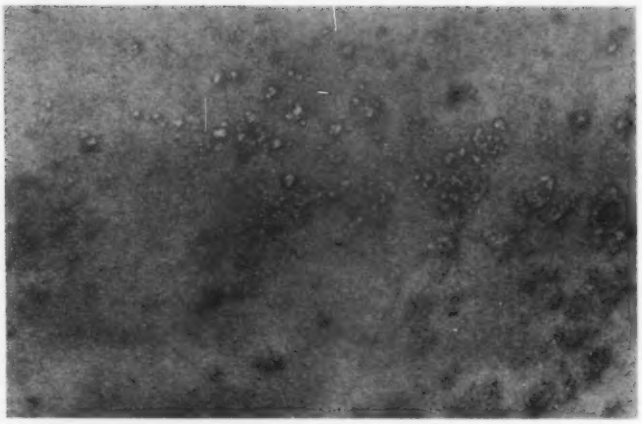


FIGURE 13. Lichen planus on the inner side of the thigh. This disease is uncommon in children. The lesions, which are flat-topped, nonscaly and of a lilac color, often are polygonal in shape and are umbilicated. They usually are very pruritic.

FIGURE 14. Lichen nitidus in a Negro boy. Note the minute, shiny, rounded papules in the flexor surface of the upper extremity. Many of the lesions were the size of a pinhead. They were not pruritic.

FIGURE 15. Lichen striatus in a four year old boy. Note the linear, lichenoid, papular eruption extending along the extensor surface of the forearm to the little finger.

losus, keratosis pilaris, lichen spinulosus, pityriasis lichenoides et varioliformis acuta, lichen urticatus and miliaria.

Treatment—As already indicated, when itching is present, it is mild as compared with that which occurs in adults. As a rule, it does not require any special treatment. The mouth should be kept clean with a mouth wash such as antiseptic solution N.F. The administration of bismuth is worth a trial. This may be administered orally in the form of BISTRIMATE® tablets,* or six intramuscular injections of bismuth subsalicylate in oil in doses of 0.5 to 1.0 cc. may be administered at intervals of one week. When bismuth is administered or-

*This preparation is supplied by Smith Pharmacal Company, Carroll Dunham.

ally, one-half to one Bistrimate tablet is given once or twice a day, depending on the age of the child. Antiphlogistic creams and emulsions (Burow's emulsion) often are useful as topical applications.

Lichen Nitidus

This condition is characterized by the accumulation of glistening, skin-colored lesions (figure 14) on the penis, lower part of the abdomen, the flexures, and elsewhere. The lesions are the size of the point or head of a pin, and they resemble sago seeds. They are very persistent, but they are not associated with itching. It is interesting that the areas of the skin affected by this type of dermatosis are often the site of the lesions of lichen planus. Indeed, some investigators believe that lichen nitidus is a variant of lichen planus.

Treatment—There is no treatment for this disease. The lesions disappear spontaneously in several months.

Lichen Striatus

Lichen striatus appears quite suddenly and extends rapidly to form a linear lichenoid band composed of small lichenoid papules (figure 15). As a rule, the eruption is self-limited, i.e., it disappears in a few weeks to several months, either spontaneously or after the application of bland medicaments. The lesions are generally unilateral and as a rule are limited to one of the upper extremities. Itching is absent. Lichen striatus should be distinguished from linear psoriasis, lichen planus and linear nevus.

Treatment—There is no specific treatment for this condition.

Postgraduate Clinical NOTES

108. ECZEMA

Acting in the part of Cleopatra, Sarah Bernhardt stabbed the slave who bore to her the tidings of Mark Antony's defeat at Actium; she stormed, raved, wrecked some of the scenery in her frenzy, and finally, as the curtain fell, dropped in a shuddering convulsive heap. As the applause died, a middle-aged British matron was heard to say to her neighbour: "How different, how very different from the home life of our own dear Queen." It is well to remember that the patient's life is different from ours: He has not seen many dermatoses, and he and his friends fear them all. In virtually every case of eczema one must give an assurance that it is not infectious, and that it must not be subjected to homely therapeutic trials; and sometimes one should say specifically that it is nobody's fault, or even that it is not a venereal disease. These small assurances may save us from the frustration of attending a patient who seems to fear us: What he really fears is that we may have discovered something about his past, and that we won't tell him.

Lastly, unlike the general physicians, when we have failed to cure our patient, we cannot hand him to the surgeons for removal of the offending organ with the confident, cheerful and very truthful assurance that he will be made worse before he is better.

R. E. Bowers, Disappointments in dermatology, *The Lancet*, January 4, 1958, pp. 43-45

Chronic simple glaucoma affects approximately 2 per cent of persons more than 40 years of age. The disease should be diagnosed by suspicion in this age group, especially in the presence of family history of eye disease, structural defect such as a small cornea or shallow anterior chamber, or vague ocular symptoms. Diagnosis may be confirmed only by tonometry. If discovered in its early stages, the condition usually may be controlled with miotic therapy.

Early Diagnosis of Chronic Simple Glaucoma

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GLAUCOMA designates eye disease characterized by increased intraocular pressure. It is of extreme importance because of its relatively high incidence, because glaucomatous visual loss is permanent, and because proper early therapy prevents visual damage. Adequate supervision of glaucoma requires a medical specialist.

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Glaucoma is present in about 2 per cent of persons over 40 years of age, an incidence similar to that of diabetes. It is estimated that 800,000 cases of undiscovered glaucoma exist in the United States today, and 12 per cent of the nation's blindness is due to glaucoma.

Chronic simple glaucoma is by far the most common type of the disease. The condition has aptly been termed "a thief in the night," because without warning it gradually and irreversibly destroys vision. It is usually painless or, at most, causes slight, occasional aching of the eyes. Complete blindness can occur without any acute attack. The elevated intraocular pressure causes slow nutritional damage, producing the characteristic arcuate scotomata which are unrecognized until they finally encroach on central vision. In its advanced stages the disease does not respond well to medical or surgical therapy and it often progresses to blindness, whereas in the early stages it usually may be controlled with miotic therapy.

It is therefore too late for action when chronic simple glaucoma is discovered as a result of the patient's complaints. Early diagnosis and preservation of vision are possible only by routine screening examinations. Glaucoma should be suspected under the following circumstances:

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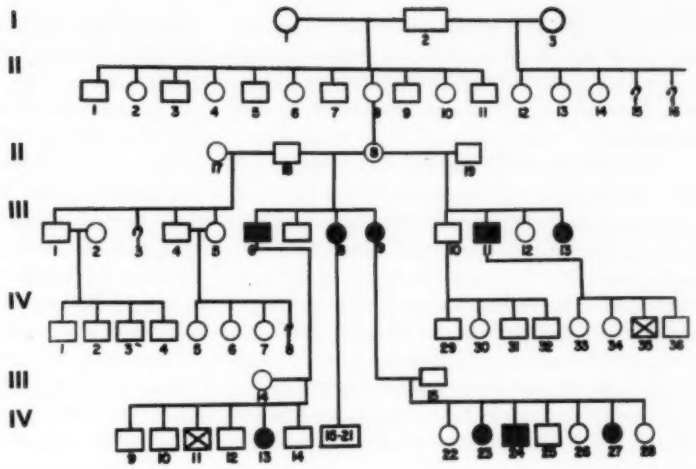

FIGURE 1. Glaucoma pedigree shows dominant inheritance.

1. If the patient is over 40 years of age.
2. If there is a family history of serious visual loss (glaucoma is hereditary).
3. If the corneal diameter is 10 mm. or less (average normal is 12 mm.).
4. If the anterior chamber is shallow and the iris seems to bow toward the cornea.
5. If the frequent, unsatisfactory changing of glasses suggests the possibility of disease.
6. If unexplained aching is present about the eyes.

The coexistence of age over 40 years and any other one of the factors listed should strongly suggest the desirability of referral to an ophthalmologist. Tonometric measurement of intraocular tension is required for accurate diagnosis. This is done routinely by most ophthalmologists in the examination of elderly patients. The intraocular pressure in chronic simple glaucoma usually is not elevated enough to permit detection by finger tension. Finger tension is easily confused with compressibility of orbital tissues, and even when done by an expert may be in error by as much as 10 mm. of mercury.

Tonometry is a simple screening procedure which is readily performed under topical anesthesia (as with a 0.5 per cent solution of PONTOCAINE® hydrochloride). Because of certain contraindications, such as the presence of eye infection or diseased corneal epithelium, tonometry should be done only after receiving special instruction in technic from an ophthalmologist. Normal tension at one reading does not guarantee the absence of glaucoma. Tensions elevated above 27 mm. of mercury require further evaluation by a variety of tests.

Chronic simple glaucoma is caused by gradually increasing resistance to the outflow of aqueous humor due to aging processes in the angle of the anterior chamber. The anatomic predisposition to glaucoma is genetically transmitted, and it is therefore most desirable to inquire about familial blindness in the routine family history. A concrete example of the value of genetic counseling is provided by the pedigree illustrated in figure 1. Individuals III 6, 8, 9, 11 and 13 became completely blind from glaucoma. Through genetic search IV 13, 23, 27 and 35 were detected as having glaucoma and were placed under therapy early in the disease. These patients have been followed for years without evidence of visual loss. By contrast, IV 10 and 24 refused to submit to examination, and both now have advanced visual loss and have begun treatment—too late!

Although certain anatomic features markedly predispose their possessors to glaucoma, its occurrence is not inevitable. It must be stressed that the great majority of patients with chronic simple glaucoma do not show

grossly visible changes of any sort. Nevertheless, it is well known that eyes with reduced corneal diameters or shallow anterior chambers have a very great predisposition toward glaucoma.

The normal adult corneal diameter is 12 mm. Inadequate development of the anterior segment of the eye, including the aqueous outflow mechanism, betrays itself by small corneal diameter—10 mm. or even less. This small cornea is present throughout the patient's life, and ordinarily does not cause elevation of pressure until sclerosing changes after the age of 40 further embarrass aqueous outflow. No matter at what age these patients with small corneas are seen, it is wise to advise them that ophthalmologic consultation in their late 30s may avert serious eye damage.

Shallowness of the anterior chamber refers to a reduced distance between cornea and iris. This characteristic is not seen in early life, and it becomes most pronounced in old age. It is probably caused by an increase in size of the lens which pushes the iris into a forward position, thereby embarrassing outflow. The forward bulging of the iris may easily be recognized as a domelike protrusion. Oblique illumination will cast a characteristic crescent shadow on the peripheral iris as illustrated in figure 2.

Sometimes it is possible to make a relatively early diagnosis of glaucoma through suspicion of vague symptoms. Patients who have had two or three pairs of unsatisfactory glasses within a short time may have eye disease rather than refractive error. (Psychoneurosis is, unfortunately, another cause for such complaints. Many glaucoma patients are tense, nervous individuals, and may at first be misdiagnosed as having a functional disorder.) Another group of patients may have vague ocular aching or discomfort, sometimes referred to the occipital region. Glaucoma should be considered as a possible cause of such unexplained discomfort in the older patient.

It is regrettable that the textbook emphasis on glaucoma suggests it should be detected by findings such as the following:

1. Reduced visual acuity uncorrectable with glasses.
2. Visual field losses.
3. Cupping and atrophy of the disk as recognized by the ophthalmoscope.

Undeniably the diagnosis can be made under

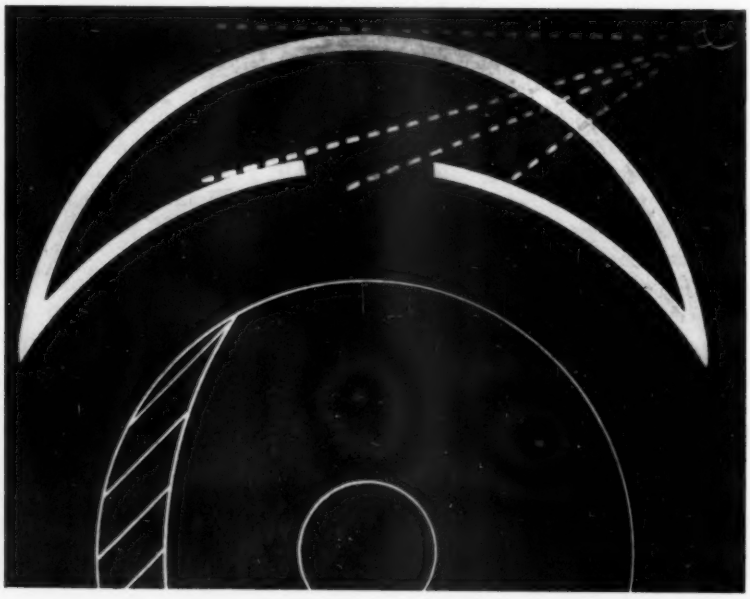

FIGURE 2. Oblique illumination casts a characteristic crescent shadow on the peripheral iris in glaucoma.

these circumstances, but it is too late. In such cases the patient will already have sustained severe and irreversible eye damage. For maximal benefit to the patient, chronic simple glaucoma must be discovered by suspicion of the disease in persons more than 40 years of age. This suspicion is increased by family history of eye disease, or by anatomic changes such as decreased corneal diameter and shallow anterior chamber, or by vague symptoms of discomfort which may lead to repeated unsatisfactory refraction checks. Confirmation of the early diagnosis is possible only by means of tonometry.

Ideally, tonometric screening should be done by every physician. I doubt that this will ever come to pass because of the demands of time and because of the great reluctance of many men to manipulate instruments about the eye. Probably the most practical solution is to refer all suspected patients to the ophthalmologist. This, of course, costs the patient money, and the referring physician is loath to cause this expense merely because of a suspicion. Bear in mind, however, that presbyopic symptoms manifest themselves in this age group. For maximal visual efficiency, most people require about three changes of glasses between the ages of 40 and 55. If these refractions are done by an ophthalmologist, the patient will simultaneously receive careful examination of his eyes for disease, including screening for glaucoma.

It is surprising how much confusion has arisen from the terminology in the field of eye care. Not only laymen, but also physicians often are unaware of the distinction between ophthalmologist, oculist, optometrist, optician and orthoptist. An ophthalmologist (or oculist) is an M.D. who has taken additional specialized training in eye care. Board certification requires three years of residency and one year of practice. He is qualified to practice in all aspects of eye care, including medical, surgical and refractive problems. The optometrist (or O.D.) is a nonmedical man, formerly often self-trained, now graduating from a college course. He is qualified to measure the refractive error of the eyes, but is not adequately trained to diagnose or treat any type of disease, ocular or systemic. The optometrist is not licensed to use drops and, therefore, cannot measure tension or dilate pupils for careful fundus examination. An optician is the technician who prepares and grinds lenses, places them in proper frames, and otherwise carries out the mechanical manufacture and fitting of glasses. The orthoptist is a medical technician who assists the ophthalmologist in the examination and care of patients with disorders of ocular movement.

With great frequency, both ocular and systemic diseases manifest themselves through visual disturbances and eye fatigue. The patient has no way to differentiate these symptoms from those of refractive error. Should he seek aid from a nonmedical refractionist, diagnosis of the true nature of his difficulty and proper treatment are often considerably delayed. In addition, the patient often loses the price of an unnecessary pair of spectacles.

One final comment is pertinent. If glaucoma were a disease which could not be modified by treatment, early diagnosis would be of little avail. The great majority of early cases do respond well to proper use of miotic therapy. By contrast, advanced cases often fail to be controlled by medical or surgical means.

Summary

Two per cent of persons over 40 years of age are estimated to have chronic simple glaucoma. This is a most insidious disease which causes serious ocular damage before the patient is aware of his disability. It should be diagnosed by suspicion in patients over 40, especially if there is a family history of eye disease, if structural defects such as small cornea or shallow anterior chamber are present (most cases do not show these structural changes), or if vague ocular symptoms occur.

Early diagnosis must be confirmed by tonometry. This is best done as routine screening by the ophthalmologist during his examination of the presbyopic patient suspected of having glaucoma.

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The mechanism by which salicylates exert their effects always has been an enigma. Because the therapeutic response to cortisone and corticotropin is similar to that obtained from salicylates, it has been suggested that the mechanism of action of the salicylates might be pituitary-adrenocortical stimulation. In this critical analysis of the evidence for and against this hypothesis, the author observes that current investigations do not indicate that the antirheumatic effects of salicylates are mediated through the pituitary-adrenal system.

A Critical Review of the Effects of Salicylates on Pituitary–adrenal Function

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ROBERT C. BATTERMAN

SALICYLATES are effective anti-inflammatory and analgesic medications for the treatment of a wide variety of arthritic conditions. Their usefulness and safety are so widely accepted that they represent "standard" drugs with which all other antirheumatic or analgesic preparations are compared. Although they have been used for centuries, first as decoctions from the bark or leaves of willow and poplar trees and since 1860 as pure chemicals, the mode and sites of action for any of the therapeutic effects are still unknown. It is true that considerable pharmacologic information has accumulated as to dosage, absorption, fate, effects on various tissues and organs, toxicity, and effectiveness for the treatment of specific conditions, but as yet the mechanisms by which salicylates exert their effects remain an enigma.

With the advent of cortisone and corticotropin, the similarity of therapeutic response between these preparations and salicylate administration in certain patients suggested that the long-sought mechanism of action of salicylates might be pituitary-adrenocortical stimulation. A review of the literature and my own observations allow a critical analysis of the evidence for and against this hypothesis.

In favor of the stimulation of the pituitary-adrenal system to explain the antirheumatic effects of salicylates, the following evidence exists.

1. Animal experiments in rats and guinea pigs suggest an increase in adrenocortical activity with salicylates. Administration of salicylates to rats depletes adrenal ascorbic acid[1-4] and cholesterol.[1] Similar results are noted with ACTH[1] and prevented by hypophysectomy.[1,3,4]

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Guinea pigs injected with salicylates show a marked elevation in plasma corticoids.[5,6] This effect also can be abolished by hypophysectomy or adrenalectomy.[7] An increased excretion of urinary 17-ketosteroids has also been observed[8] in these animals.

2. A mild "Cushing" syndrome has been reported[9] in a 13 year old patient with rheumatic fever following prolonged administration of aspirin.

3. In accordance with the eosinopenia noted with ACTH administration, suggestive of pituitary activity, a similar response on circulating eosinophils has been reported in rats,[1] guinea pigs,[8] and man[10,11] following large doses of salicylates. Hypophysectomy[1] and adrenalectomy[12] abolished this effect in rats. The eosinopenic effect of salicylates in man was not confirmed.[13,14]

4. Studies in man, although conflicting because of numerous variables such as utilization of normal subjects and patients with rheumatic fever or rheumatoid arthritis, adults and children, and various doses and routes of administration of different salicylates, are fundamentally concerned with changes in plasma concentration of corticoids and urinary excretion of neutral 17-ketosteroids and corticosteroids. Van Cauwenberge and Hensghem,[15] reporting on eight patients (four with acute rheumatic fever, two with rheumatoid arthritis, one with ankylosing spondylitis, and one with fibrositis and endarteritis), noted that the administration of aspirin in doses of 1 gm. every three hours for eight days to several weeks resulted in an increased excretion of reducing steroids but not 17-ketosteroids. Other studies, as indicated later, do not confirm these observations. A recent report[16] also noted a "consistent increase in neutral 17-ketosteroid excretion and both free and conjugated corticosteroid excretion" with aspirin ingestion in both normal subjects and patients with rheumatoid arthritis. The implication in this report, however, favors a nonadrenal pituitary effect to account for the results. High plasma levels of phenylhydrazine-reacting steroids have been noted[5] with salicylate intoxication in children, but this may represent a nonspecific stress reaction to toxicity rather than an effect of the administration of salicylates per se.

The evidence, therefore, in favor of the adrenal-pituitary stimulation to account for the antirheumatic effects of salicylates is meager and concerned with unusually high nontherapeutic doses in rats and guinea pigs, the unconfirmed eosinopenic responses in man, and questionable alterations of steroid blood and urine levels. On the other hand, considerable evidence has accumulated to negate any hypothesis that the anti-inflammatory and antirheumatic effects of salicylates are mediated through the pituitary-adrenal system.

1. Contrary to the elevated plasma corticoids observed in guinea pigs,[5,6] decreased levels have been noted in dogs.[16] Species differences might be the explanation.

2. Animal and clinical experiments indicate that the effects of salicylates are not only unlike cortisone or pituitary stimulation but also exactly opposite. Thus, cortisone inhibits wound healing, as judged by standard skin wounds in mice, but salicylates do not.[17] Ingle and associates[18,19] demonstrated that in partially depancreatized rats cortisone exacerbates the diabetes whereas aspirin decreases glycosuria. Similar results[20] have been obtained in alloxan-diabetic rats. In man it has been known since 1875 that salicylates possess a hypoglycemic effect and might be of benefit for patients with mild diabetes mellitus. Reid and co-workers[21] recently demonstrated this effect. Corticosteroids may aggravate or produce permanent diabetes mellitus in patients who receive them for an extended period. Prolonged administration of cortisone elevates blood uric acid in man and may induce gout,[22] whereas salicylates exert a well-recognized uricosuric effect. In man, salicylates increase the prothrombin and clotting times[23] but cortisone and ACTH have the opposite effect.[24] The treatment of a wide variety of musculoskeletal conditions by means of chronic administration of salicylates or steroids alone or in combination has resulted in therapeutic paradoxes suggestive of mutual antagonistic effects.[25] After an initial satisfactory antirheumatic or analgesic effect, or both, the responsiveness of both medications diminishes as

therapy with combinations continues. The data reported by Herndon and associates[16] also suggest this phenomenon.

3. The implication that the depletion of adrenal ascorbic acid in rats represents an antirheumatic effect secondary to pituitary stimulation is not warranted. This effect is nonspecific and can be produced by drugs that do not possess antirheumatic activity.[26]

4. Many drugs, such as aminopyrine, gentisic acid and cinchophen, exert marked antirheumatic effects and yet do not alter pituitary-adrenal function in animals.

5. The eosinopenic effects of salicylates in man have not been confirmed,[13,14] and the results reported by Roskam and Van Cauwenberge[11] are questionable since "spontaneous" alterations in eosinophil counts are marked during the hours used by these investigators.

6. Adrenal function is not required for salicylate action. Ungar and co-workers[27] demonstrated that the anti-inflammatory effects of salicylates occur in hypophysectomized and adrenalectomized animals. Peterson and associates[28] noted the beneficial effects of salicylates in a rheumatoid patient in spite of suppressed adrenal function. The same authors cited an observation by Thorn of the anti-inflammatory response of salicylates in patients with Addison's disease.

7. Therapeutic doses, either single or multiple, exert no effect on plasma level of 17-hydroxycorticosteroids in normal adults,[28] patients with acute rheumatic fever,[29] or patients with rheumatoid arthritis.[28,29] A lowering of plasma corticoids rather than an increase was noted by Done and co-workers[30] for normal subjects, and recently Herndon and associates[16] noted this effect for normal subjects and patients with rheumatoid arthritis, and Seely and associates[31] for patients with rheumatic fever. Aspirin decreases the response of corticotropin infusion on plasma corticoid levels in both normal subjects and patients with rheumatoid arthritis.[16] This is an opposing effect of salicylate on "pituitary stimulation."

Urinary excretion of corticosteroids or 17-ketosteroids following administration of salicylates was not altered in normal subjects,[28,30] patients with rheumatic fever,[31-33] or patients with rheumatoid arthritis.[28,32] On the other hand, Herndon and associates[16] noted that aspirin increased urinary excretion of neutral 17-ketosteroids and both free and conjugated corticosteroids. Aspirin also increased the excretion of free reducing steroids following infusion of corticotropin but decreased the excretion of neutral 17-ketosteroids.

The bulk of the evidence to date, attained by newer and more accurate technics, does not support the hypothesis that salicylates exert their antirheumatic and anti-inflammatory effects secondary to alteration of the pituitary-adrenal system. Regardless of mechanism of action, salicylates are effective, safe medications for the symptomatic relief of a wide variety of arthritic conditions. Their utilization, with due regard to type of preparation, dosage, routes of administration and chronic nature of the conditions being treated, will assure the physician uniformity and reliability of relief in the majority of patients.

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Total cardiopulmonary by-pass by means of the pump-oxygenator is now a safe, reliable technic and allows surgical correction of many intracardiac lesions. Direct-vision surgical procedures are carried out at normal body temperature, with optimal function of the heart and body. Ventricular septal defect and tetralogy of Fallot are the most commonly encountered lesions and are included in the four case histories presented to illustrate methods of preoperative evaluation and application of technics.

Open Heart Surgery Using Total Body Perfusion

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THE use of a pump-oxygenator to provide total cardiopulmonary bypass and thus allow direct-vision intracardiac surgery is no longer an experimental procedure.[1] There still are many problems to be solved, but in the treatment of many intracardiac lesions it can truly be said that this technic is safe, reliable and in everyday use in many centers. Although effort was at first concentrated on treatment of congenital heart disease, the desirability of using a direct-vision technic in treatment of many forms of acquired heart disease is apparent and an increasing application in this field has developed.

The pump-oxygenator used for these procedures is illustrated in figure 1.[2,3] It is constructed mainly from polyvinyl plastic tubing. Siphonage through plastic cannulae inserted in the venae cavae through the wall of the right atrium completely diverts to the pump-oxygenator venous blood returning to the heart. This blood is pumped into the vertical mixing tube of the oxygenator where it is filmed on the surfaces of streams of oxygen bubbles. As the blood ascends in this tube it is fully oxygenated and excess carbon dioxide is released. The blood then passes into an obliquely placed chamber in which debubbling is accomplished by momentary contact with a siliconized surface. Further debubbling of the blood is achieved as it gravitates into a helical reservoir placed in a thermostatically controlled water bath. The latter maintains the temperature of the blood in the extracorporeal circuit. After passage through a filter, the blood is returned to the patient's arterial system by way of the femoral or subclavian artery. Blood collecting in the heart during the period of the cardiotomy is returned to the oxygenator and used again. It has been possible to bypass the heart and lungs completely for more than 90 minutes using this apparatus, thus allowing precise and unhurried repair of an intracardiac defect.

Use of this apparatus has enabled complete surgical correction of a wide variety of cardiac

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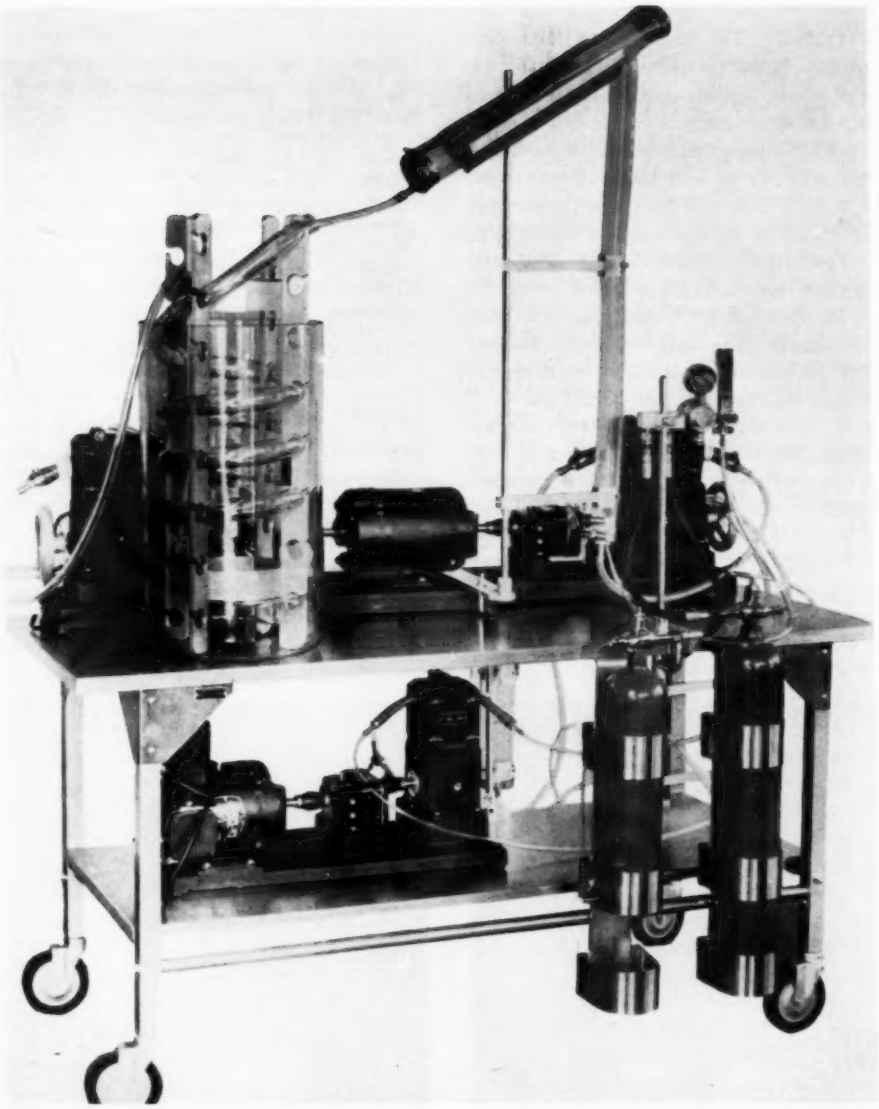

FIGURE 1. The helix reservoir pump-oxygenator. Venous blood drains by gravity to the venous reservoir (lower shelf, extreme right), from which it is pumped to meet an oxygen stream in the vertical mixing tube. The oxygenated blood is then debubbled in the obliquely placed chamber. From there the blood flows into a helical reservoir in the glass water bath. This helical reservoir serves several purposes: (1) It completes separation of the oxygenated blood from any small bubbles or free gas that may have passed from the debubbling tube. The free gas has a lesser density than whole blood. By the character of spiral descent the heavier whole blood flows in a laminar fashion beneath the free gas which is displaced upward. (2) Normal body temperatures are maintained by the helical coil in a constant-temperature water bath. (3) The coil serves as a reservoir for the oxygenated blood until time for its use. (4) The upper meniscus of blood serves as a level indicator to balance the input and output of the oxygenator.

Blood is returned to the patient by the "arterial" pump head (extreme left, upper shelf). The cardiotomy reservoir, mercury trap and pump are shown on the lower shelf. The blood from this source is also processed in the vertical mixing tube. The double mixing tube and debubbler system is used for perfusions requiring larger quantities of blood (2500 cc. of blood per minute and up).

lesions (table 1). The lesion most commonly involved has been ventricular septal defect. Despite the fact that in many of these cases operation has been carried out at a late stage in the disease's progress, operative mortality has been reduced to less than 10 per cent. Tetralogy of Fallot has been the next most common lesion requiring surgical correction, and the operative mortality is now less than the long-term mortality reported by many workers for the palliative procedures of systemic-pulmonary anastomosis[4,5] and transventricular infundibular resection which formerly were used in treatment of this condition.

We have selected four case records to illustrate the application of these technics and to present some of the methods of preoperative evaluation.

TABLE 1

CARDIAC LESIONS CORRECTED SURGICALLY THROUGH USE OF TOTAL CARDIOPULMONARY BYPASS

Congenital lesions:
Ventricular septal defect
Atrial septal defect
Atrioventricularis communis
Aorticopulmonary window
Pulmonary stenosis
Aortic and subaortic stenosis
Tetralogy of Fallot
Pulmonary atresia
Tricuspid stenosis
Anomalous pulmonary venous drainage
Cor triatriatum
Transposition of the great vessels
Ebstein's disease
Acquired lesions:
Mitral stenosis
Mitral insufficiency
Aortic stenosis
Aortic sinus aneurysm
Ventricular aneurysm
"Myxoma" of left atrium
Aneurysm of thoracic area

Case 1: Ventricular Septal Defect[6]

A 10 year old white boy had frequent upper respiratory infections and twice was

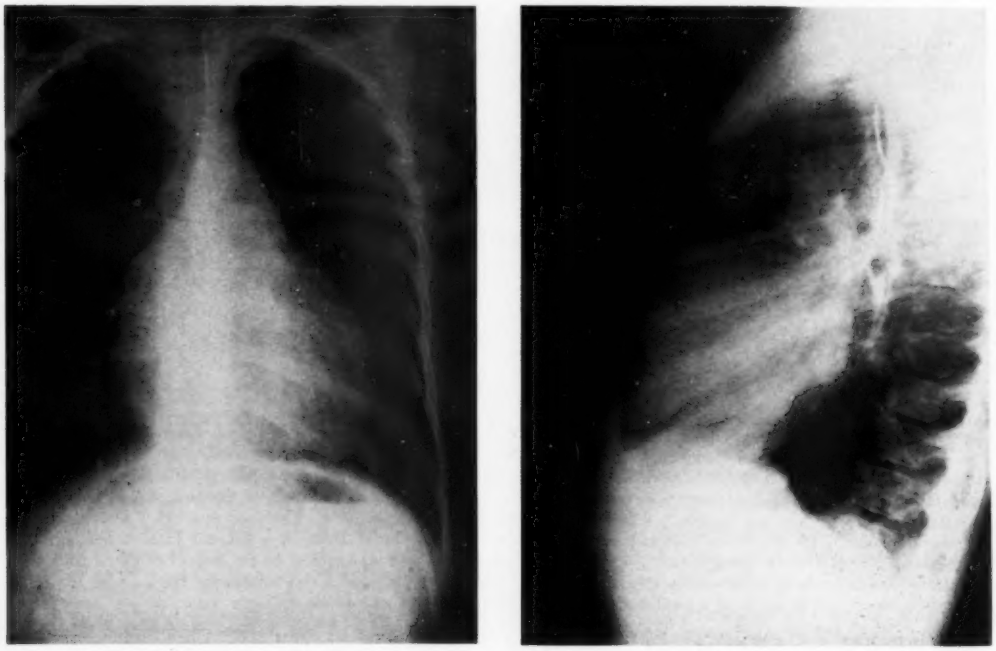

FIGURE 2. Case 1. Preoperative chest roentgenograms showing increased pulmonary vascularity, prominence of pulmonary artery segment, right ventricular hypertrophy, and left atrial enlargement.

hospitalized because of severe respiratory tract infection. His development had lagged behind that of other boys his age, and he weighed 50 lb. His activity, however, was only slightly limited, and he had never evidenced cardiac decompensation, cyanosis, syncope or convulsions. He was not in obvious distress, and significant physical findings were confined to the heart. Cardiac activity was markedly increased, and one could feel a heave in the second left interspace. Auscultation revealed a systolic murmur over the entire precordium but with maximal intensity in the third left interspace. There was a short mid-diastolic rumbling murmur confined to the apex. The pulmonary second sound was markedly accentuated. The electrocardiogram showed evidence of both right and left ventricular hypertrophy. Fluoroscopic examination of the chest disclosed greatly increased vascularity of the lung fields. The pulmonary arteries were enlarged and pulsated actively. There was moderate cardiac enlargement involving the right ventricle, probably the left ventricle, and left atrium (figure 2).

Cardiac catheterization had been done when the boy was eight years of age. The main features were a pulmonary artery pressure of 95/48 mm. Hg, right ventricular pressure of 95/0, a three volume jump in oxygen saturation at the ventricular level, and femoral artery oxygen saturation of 91 per cent.

From these studies a diagnosis of ventricular septal defect with advanced pulmonary hypertension was made.

Operation—Anterior bilateral thoracotomy provided access to the heart. Total cardiopulmonary bypass with the bubble oxygenator was utilized for 22 minutes to allow the surgeon to effect a complete repair of a ventricular septal defect 3½ cm. in diameter. Pressure in the pulmonary artery at operation but before closure of the defect was 67/40 mm. Hg when the aortic pressure was 77/62 mm. Hg. Immediately after closure of the defect, pulmonary artery pressure was 36/16 mm. Hg; aortic pressure was 84/55 mm. Hg. The patient recovered rapidly and completely from the operation and was dismissed from the hospital on the twenty-first postoperative day. At that time, no murmur was audible over the precordium.

Case 2: Tetralogy of Fallot[7]

A full-term white baby progressed well during the first month of life but then displayed cyanosis which became increasingly severe as the weeks passed. At the age of three months he began to have convulsions and attacks of syncope as often as three times daily. For three months prior to surgical treatment, he lived in an oxygen tent, and his condition deteriorated alarmingly if he was removed from it for even short intervals. At the age of seven months he was a cyanosed, underdeveloped child in considerable respiratory distress. Blood pressure was 60 mm. Hg in the arms and legs by the flush technic. There was no evidence of cardiac enlargement. The pulmonary second sound was clearly heard, and there was a systolic murmur at the left sternal border. The liver was palpable 2 cm. below the right costal margin. The hemoglobin was 15.5 gm. An electrocardiogram showed an electrical axis of the heart of 135 degrees and right ventricular hypertrophy. A roentgenogram of the chest (figure 3a) showed a heart of normal size. The apex was rounded and elevated, suggesting right ventricular hypertrophy. Pulmonary vascular markings were diminished.

Angiocardiography had been carried out at the age of three months, and revealed successive filling of the right atrium, right ventricle, and simultaneously the aorta and pulmonary artery (figure 3b).

The right ventricular outflow tract was narrowed just below the valvular plane and the pulmonary arteries themselves were small. The aorta which filled from the right ventricle was of larger diameter than normal and the arch was on the right side.

These findings were considered typical of tetralogy of Fallot.

Operation—In view of the severe symptoms and the progressive deterioration of the patient's general condition, the decision was made to operate at the early age of seven months. Operative findings were typical of tetralogy of Fallot. Using the pump-oxygena-

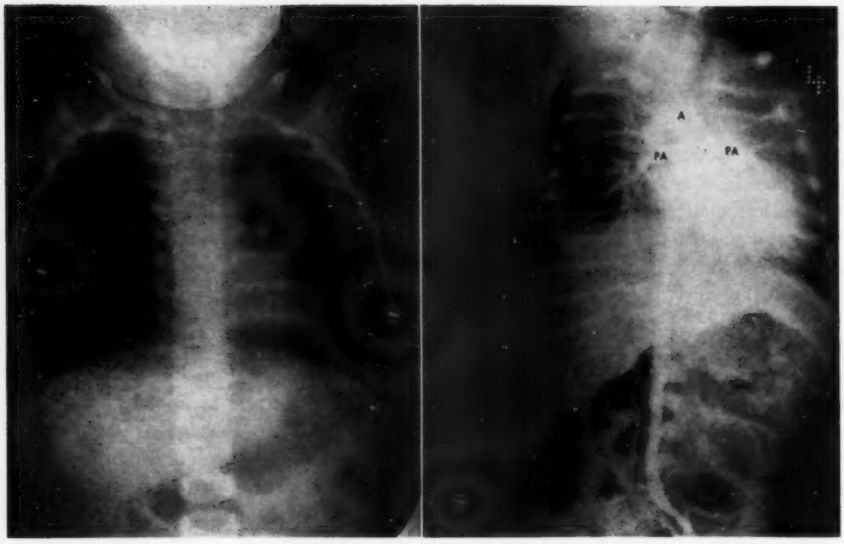

FIGURE 3. Case 2: a *(left)*. Posteroanterior chest roentgenogram showing typical coeur en sabot with decreased pulmonary vascularity. b *(right)*. Angiocardiogram showing simultaneous filling of the large aorta and small pulmonary artery. The narrowed infundibulum of the right ventricle also can be seen.

FIGURE 4. Case 2. Three months after operation. Posteroanterior chest roentgenogram shows some increase in heart size and a striking improvement in pulmonary vascular marking.

tor to provide total cardiopulmonary bypass for 13 minutes, the ventricular septal defect was closed with interrupted silk sutures tied over a pledget of polyvinyl sponge. The tissue producing the infundibular pulmonary stenosis also was resected. The small patient made a gratifying recovery, displaying a healthy pink color and being free from convulsive and syncopal attacks (figure 4). Recently, when he was two and one-half years of age, his case was reviewed. He was a healthy pink child who "ran around actively all day." A soft systolic murmur was audible at the left sternal border. A specimen of blood taken from the femoral artery at the age of 15 months showed an oxygen saturation of 100 per cent.

Case 3: Rupture of Aortic Sinus Aneurysm Into Right Atrium[8]

During a routine physical examination at the time of discharge from the armed services a 35 year old man was found to have a systolic murmur. He was in excellent health at the time. He continued to be in good health until six months before he was admitted to the University of Minnesota Hospitals, when he experienced the sudden onset of dyspnea on slight exertion. His personal physician examined him and found both a systolic and a diastolic murmur best heard at the lower end

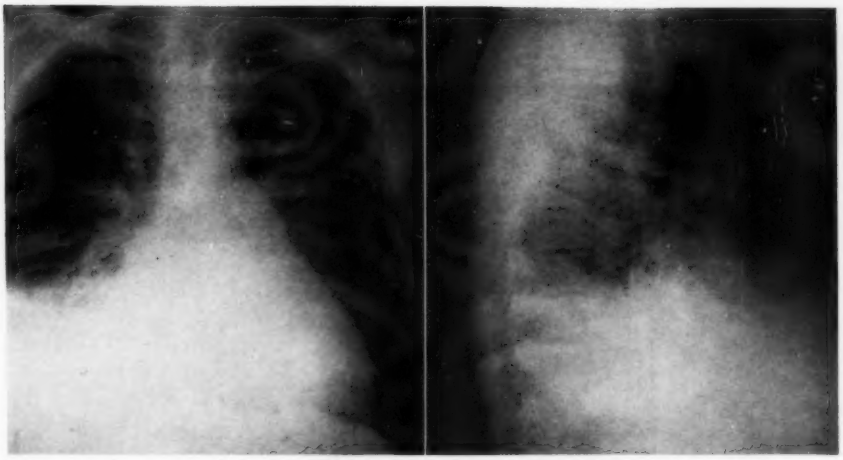

FIGURE 5. Case 3. Posteroanterior and lateral roentgenograms of the chest taken one month before operation. The increased heart size, pulmonary plethora and right pleural effusion can be seen.

of the sternum. Despite careful medical care with bed rest, digitalis and mercurial diuretics, his condition progressed rapidly to severe and intractable congestive heart-failure.

Notable physical findings at the time of admission to the University of Minnesota Hospitals were a collapsing pulse, blood pressure of 160/40, orthopnea, distention of the jugular vein to the angle of the jaw, and bilateral pleural effusion. The apex beat was felt in the sixth left intercostal space 4 in. from the midline. The pulmonary second sound was markedly accentuated. A harsh systolic and diastolic murmur could be heard over the entire precordium, loudest in the fourth intercostal space at the left border of the sternum. The liver could be felt 5 cm. below the right costal margin. There was gross edema of the sacrum and both lower extremities. The electrocardiogram showed left axis deviation and ST-T changes consistent with digitalis administration. Chest roentgenograms (figure 5) disclosed marked cardiomegaly involving both ventricles with moderate left atrial enlargement. There was moderate prominence of the pulmonary artery segment. Bilateral pleural effusions were present.

Table 2 gives the data obtained by cardiac catheterization four months before the patient was admitted to the hospital.

The diagnosis made was rupture of an aortic sinus aneurysm into the right atrium. Immediately before operation, 1500 cc. of straw-colored fluid was removed from the left pleural cavity by thoracentesis.

TABLE 2

FINDINGS ON CARDIAC CATHETERIZATION, CASE OF RUPTURE OF AORTIC SINUS ANEURYSM INTO RIGHT ATRIUM*

	OXYGEN SATURATION *(Vol. per cent)*	PRESSURE *(Mm. Hg)*
S.V.C.	9.34	
Right auricular (high)	10.9	Mean 17
Right auricular (mid)	15.5	
Right auricular (low)	15.1	
Right ventricular (low)	15.4	38/3
		Mean 20
Right ventricular (high)	15.7	
Pulmonary artery (right)	15.3	38/23
		Mean 30
Pulmonary artery (left)	15.5	
Pulm. cap.	17.9	
Brachial artery	18.01	

Oxygen uptake, 27/4 cc. per minute
Oxygen capacity, 18.3 vol. per cent
Systemic flow, 3.8 l. per minute
Pulmonary flow, 10.1 l. per minute

*For a description of this case, see the text.

Operation—Total cardiopulmonary bypass was used for 17 minutes, and the heart was arrested with potassium citrate solution for eight minutes. The right atrium was opened widely. A fingerlike projection 10 cm. long and 2 cm. in diameter was seen protruding into the lumen of the atrium from a point on the posterior wall 1 cm. above the annulus of the tricuspid valve. The end of the fingerlike sac showed a perforation 1.5 cm. in diameter. The sac was excised and the deficiency in its base was closed with interrupted silk sutures,

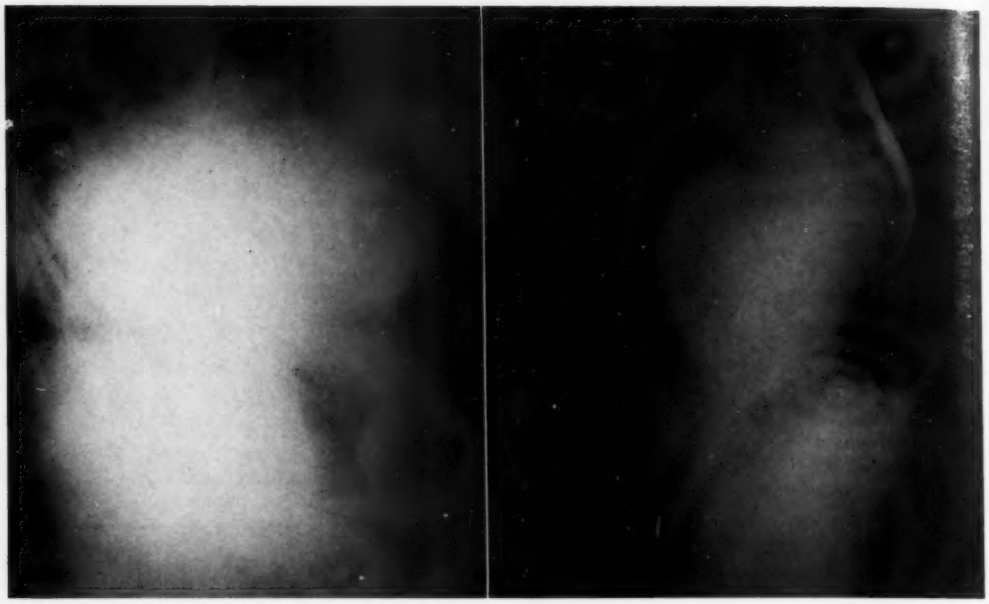

FIGURE 6. Case 4. Posteroanterior and lateral chest roentgenograms taken before operation showing the "giant" left atrium of advanced mitral insufficiency.

thus closing the site of origin of the aortic sinus aneurysm. The atriotomy was repaired. It was noted that the diastolic blood pressure rose to 90 mm. Hg immediately after closure of the defect. The patient recovered rapidly and dramatically and was dismissed from the hospital four weeks after operation. An interesting feature of his convalescence was the occurrence of marked diuresis in the first 14 days. His weight fell 23 lb. in the first 10 days. Murmurs could not be heard over the precordium at the time of his dismissal. Six months after operation he continues to be in good health.

Case 4: Rheumatic Mitral Insufficiency[9]

A 19 year old white woman was referred for open heart surgery because of severe limitation of activities with dyspnea on exertion and frequent attacks of paroxysmal nocturnal dyspnea. She had had two acute attacks of rheumatic fever, the first at eight years of age and the second at 14. After the second attack she had repeated attacks of cardiac decompensation which were only partially controlled by bed rest, digitalis and mercurial diuretics.

Physical examination showed severe wasting of the extremities and edema of the ankles. Pulse was irregular, the rate being 100 beats per minute. Blood pressure was 130/80. There was a very forceful apical heart beat 10 cm. from the midsternal line in the fifth left intercostal space. A systolic thrill was felt widely over the precordium, maximally at the apex. On auscultation a grade 4 systolic murmur was heard, maximally at the apex and transmitted laterally and posteriorly. A short early diastolic murmur, rumbling in quality, also could be heard localized to the apex. The liver was felt 5 cm. below the right costal margin. An electrocardiogram showed auricular fibrillation and a left ventricular "strain" pattern. Pulmonary congestive changes were seen on the chest roentgenograms. The heart was grossly enlarged with a "giant" left atrium (figure 6).

Operation—Exposure was provided by a right lateral thoracotomy through the bed of the fifth rib. The left atrium was seen to be

greatly distended. It bulged backward and laterally, displacing the right atrium forward. There was an obvious expansion of the atrium with each ventricular systole which was easily visible and palpable. The lungs showed scarring from prior infarction. Preliminary digital exploration of the right atrium revealed some thickening of the tricuspid leaflets but no stenosis or regurgitation.

To visualize the mitral valve, the heart and lungs were bypassed using the bubble-oxygenator for 29 minutes and a left atriotomy was made. The mitral valve was well seen and with the heart still beating a good idea of its function could be gained. There was gross mitral incompetence due almost entirely to dilatation of the annulus. The valve cusps, though widely separated, were supple and of good area and showed no deformity. Sutures were placed through the annulus adjacent to the valve commissures, and when these were tied down, thus narrowing the annulus, the valve cusps apposed each other and there was no longer a regurgitant jet with each ventricular systole. After closure of the heart, thrills could not be felt over the left atrium. The patient recovered rapidly and was dismissed from the hospital 30 days after operation. Only a very faint systolic murmur could be heard at the apex. Six months after operation she manifests a striking and progressive improvement.

Summary

Many persons can now be salvaged from the ravages of intracardiac lesions which only a few years ago led to premature death. Direct-vision intracardiac surgical procedures are being done with increasing safety especially when compared with the danger in leaving these cardiac lesions untreated.

Perfusion technics are invaluable as an aid to the surgeon in performing these open intracardiac operations. The surgical procedures are done at normal body temperatures, which maintain the heart and body at optimal functioning state. The surgeon may have all the time that is necessary to accomplish some of the more complicated plastic repairs inside the heart in an unhurried fashion.

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Clinical material from five cases is presented in this discussion of postpartum depression in normal women. Favorable results were achieved by a preventive technic consisting of (1) familiarizing the pregnant woman with the unavoidable resuscitation of repressed infantile fears during pregnancy, contrasting these with harmless reality, and (2) pointing out that in refusing to admit these fears to herself she engenders postpartum depression. The author suggests that the general practitioner and obstetrician may practice this technic.

Psychoprophylaxis of Postpartum Depression

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THE psychoanalytic literature has repeatedly emphasized that the motives of postpartum depression are "numerous and not always clear" (H. Deutsch, "The Psychology of Women," II, page 249). Different phenomena have been adduced: fear of death, exhaustion, pain, absence of identification with the woman's mother, rebellion against the feminine role and motherhood, rejection of the child or husband, disturbance of the fantasies built up during pregnancy, separation and castration fears, inner guilt, the use of modern forms of anesthesia which exclude the woman from conscious participation in the birth and thus deprive her of the opportunity of placing masochistic depositions, etc. Still, wisdom's last word is the statement that "there is an increasing number of women who, without being actually neurotic, nevertheless behave in an unusual fashion after a technically perfect painless delivery" (Deutsch, *loc. cit.*, page 251). This phenomenon is so typical that Deutsch suggested modifying the old saying *Omne animal post coitum triste est* to *Omnis mulier post partum tristis est*, though the joy of motherhood may appear after the "sad disappointment" (page 249).

In his valuable pioneer work, "Psychosomatic Gynecology," William Kroger (in collaboration with Freed) collected the extensive literature on the topic, stressed the connection with frigidity, and correctly remarked that "pregnancy serves to bring into sharp relief these women's neurotic conflicts, even though these individuals were apparently well adjusted prior to pregnancy" (page 113).

In this discussion of the problem I am deliberately omitting the more complex phenomena of full-fledged postpartum neuroses and

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psychoses, in which a diseased personality uses the birth experience as a catalyst for aggravation of a state previously present but latent. These are extremely technical problems and belong in the realm of psychopathology. I am concentrating exclusively on women who are *not* neurotic, or not too neurotic, and who, despite a not-too-difficult delivery and a well-defined ability for maternal love, nevertheless go through a postpartum depression. In short, I am speaking about *normal women*.

The psychiatrist does not have an opportunity to observe transitory, "harmless" postpartum depression. If transitory, though painful, these depressions correct themselves in just a few days or a few weeks. Usually the psychiatrist is called on to treat only the longer-lasting neurotic and psychotic postpartum clinical pictures. On the other hand the obstetrician, with few exceptions, lacks psychiatric knowledge and is glad not to be bothered by these "unreasonable," seemingly hysterical phenomena or can offer reassurance only. But the women suffer none the less.

There is, however, one situation in which the psychiatrist has the opportunity to observe precursors of these fears and depressions *before* they fully materialize. This is when he happens to be treating a mildly neurotic woman during her pregnancy, the woman having come into analysis because of personality conflicts unrelated to the birth-giving situation. I have treated three women under these conditions. After interruption of treatment during their confinement, all three returned to analysis, and it was possible to check the results of the *preventive treatment* which I shall advocate. Postpartum depression did not develop in any of these three cases. Admittedly these women became pregnant under favorable conditions—after solving their neurotic conflicts with their husbands.

I have also had the opportunity of seeing in consultation, once or twice, two pregnant women who could not enter treatment at that time. The same preventive technic was applied in their cases. The results were favorable, they subsequently reported to me.

These five cases have given me the idea of suggesting, in simplified form, the preventive procedure to be outlined.

Pregnancy, and especially the act of giving birth, mobilizes (as all dangers do) repressed *infantile* fears present in everybody. These fears are unconscious and totally irrational. This "septet of baby fears," as I called it in "The Basic Neurosis," comprises such fantastic entities as fears of being starved, devoured, poisoned, choked, drained, chopped to pieces, and castrated. All these fears have one common denominator: The fear-sufferer is on the *passive-masochistic* end—in short, he is the victim. It is true that later in life these fears disappear from consciousness and are transformed into more "rational" forms. Study of neuroses proves their presence. Whatever neurotic entity the psychiatrist touches, infantile fears come to the fore, under the analytic microscope. Of course, skeptics claim that these fears are only in the psychiatrist's mind and therefore he projects them onto the patient. This is a convenient joke, but facts are still facts. The older Huxley averred the ironic dictum: "Science is a beautiful theory killed by an ugly fact." This justifiably skeptical view of premature pet-theories does not shut out the possibility that sometimes ugly facts are observed first, and secondarily elevated to a theory.

What fears, specifically, are thrown to the psychic surface in situations of danger, and then secondarily rationalized, will depend on the individual and the quantity and quality of his undigested baby fears. In these critical periods his "once upon a baby time" becomes his very real present.

It was Freud who stated that somewhere fear lurks behind all neurotic manifestations. In the specific fears connected with parturition the following fears of the past are activated: fears of being drained, choked, chopped to pieces, eviscerated (castrated). If one goes back to the baby situation and is familiar with the background of these fears, one can well understand why this should be so.

The fear of being drained stems, paradoxically, from the child's misconceptions of defecation and urination. The infant does not know that waste matter must be eliminated.

As he sees it, parts of his body are taken away from him by a power stronger than himself, a mechanism that terrifies the child and offends his megalomania to boot. During birth, expulsion of the child is inwardly identified with anal mechanisms. It is well known that all children go through a phase in which the anal opening is considered the sexual aperture. Kroger (*loc. cit.*, pages 109 and 110) has correctly registered cries of distress uttered by such women before giving birth: "I feel like my bowels are going to move; I'll probably make a terrible mess! Please let me go to the toilet." This is not simply a transitory "anal regression" but is a regression to something deeper: a baby fear of more terrifying nature.

The fear of being chopped to pieces has a no less paradoxical humble beginning, namely, the handling of the baby during cleaning and washing procedures. The newcomer to this world finds the mother's purposes obscure. No matter how tender and careful the mother is, from the child's viewpoint the manipulations are terrifying. Later, all manipulations with surgical purposes are subsumed under this heading.

Fear of evisceration, later subsumed under castration fear, is the culmination of all baby fears. Numerous variations are encountered. Later these are also connected with lack of anatomic congruity between male and female genitalia.

One could go into additional detail and show how every infantile fear has a representation during pregnancy. For example, the vomiting during early pregnancy, although some authors believe there are toxic reasons, certainly has a psychic superstructure as well —the fear of being poisoned. The oral conception is nullified through oral expulsion. And breathing difficulties caused by ascension of the uterus during pregnancy activate old fantasies of being choked. Other examples could be adduced.

One should also mention that baby fears are later shifted to masturbation and guilt toward mother. Hence the spectacle of so many pregnant women afraid of giving birth to a crippled or moronic child. Added to all this are exhibitionistic fears. The girl's entire education emphasizes the idea of modesty. All at once, during pregnancy, and especially during the process of giving birth, the rules of "decency" are suspended. Not only physicians and nurses but even outsiders are involved, for during the last months pregnancy cannot be hidden.

To demonstrate the fantastic tricks the unconscious (the hidden child in the adult) can play, I am adducing the example of a business woman treated nearly 30 years ago. She sought analysis because of a bizarre phobia that a lion would attack her from behind in the dark. She could not remain alone at home evenings and was fearful of going out. "Don't tell me, please," she begged, "that there are no lions running around in apartments in this modern city. I know that my fears are stupid and irrational." She expressed preference for a treatment hour directly after lunch: "I suffer from an old stomach disorder and have cramps after every meal. Since I have to lie on a couch for analysis, I thought that to save time I could combine my midday rest with analysis." She was impatient with me when I tried to get some information about her "purely organic" stomach troubles. (This analysis took place before the advent of psychosomatic medicine.) She informed me that with every meal she had "peculiar" cramps in her bowels. Rest relieved distressing flatulence, and after her rest (ending with a "big flatus") she felt "like a newborn person."

Analysis disclosed her fear of being attacked by a lion to be a banal oedipal rape fantasy. When she was three years old her father, a Herculean man, had taken her to the zoo. She admired the lion. "He is nearly as big as you are," she told her flattered father. She wanted to feed the lions from her lunch box but the father warned her that this would be dangerous. The substitution of lion for father was easily established. An attack from behind corresponded to her infantile fantasy that the anus was the female sex organ.

So far this is a commonplace anxiety hysteria. More interesting was the psychogenesis of her gastrointestinal symptoms. Eating proved to be a thinly disguised sexual fantasy.

Each meal was an oral impregnation. The orally conceived baby developed in the bowels, and following labor pains (cramps) was delivered per anum (flatulence). It was psychologically quite appropriate that she felt "like a newborn person." This hysterical materialization of the typical childish fantasy of oral conception, intestinal pregnancy and anal birth (the genitalia were totally excluded) was consummated in one hour, three times daily. In addition to the complete disregard for the realities of time, and in addition to anatomic absurdities, other evidences of infantile omnipotence were the multitude of "children" she "produced" (no less than 1,095 in the course of a year). In this way she won the "competition" with her mother, who was able to produce no more than a single child a year.

Now, all these apprehensions, normally dormant in repression, were "once upon a baby time" connected with some uncanny unconscious pleasure—the pleasure in fear, psychic masochism. Since these apprehensions come alive (one can adduce Homer's poetic simile of the Greek heroes in Hades who were resuscitated when they drank blood) the defense sets in too. Thus, as bottom, all fear is directed against the masochistic inner danger and allure; it is only later that the fear is rationalized (because the origin is not conscious) in terms of reality dangers confronting the woman during birth giving.

This also explains the omission from the list of baby fears of the most logical one, the fear of death. Freud's opinion that fear of death is not represented in the unconscious has been confirmed time and again. In the unconscious, death means suffering, loneliness, being left helpless in the cold, immobility—once more the paraphernalia of psychic masochism.

The preventive technic advocated here consists of two parts:

1. *Familiarizing pregnant women beforehand (during the last months of pregnancy) with the unavoidable resuscitation of repressed infantile fears during pregnancy and parturition*, contrasting these with the harmless reality situation. Reassuring statements that "everything will be all right" are quite insufficient. The obstetrician or general practitioner who will assist the woman during the birth-giving process can mention the baby fears previously enumerated. Only in severe and unmanageable cases should the woman be sent to a psychiatrist.

2. Familiarizing pregnant women with the fact that in refusing to admit their fears to themselves *they are mortgaging their happiness in the period after birth of the child and will pay the price of postpartum depression.* Once inner fears, covering psychic masochism, have been mobilized, they cannot be dismissed, they inundate the personality. This is a new discovery, first stated in my book, "The Superego," published in 1952.

The latter statement requires elaboration. If one takes a vacation or pleasure trip and allots X dollars to cover expenses, and returns from the trip having spent less than expected, the surplus funds are generally returned to the savings account. The money was prepared, not spent, and saved. The situation is quite different with psychic energy. Once prepared, it *must* be spent, though in different disguises. This peculiar fact applies also to masochistic deposits and can be demonstrated in the phenomenon called "crying because of happiness."* Nothing is more paradoxical than a person shedding tears when joy is expected. Viewed psychiatrically the story is less grotesque. A happy event, or even a conspicuously felicitous event calling for the comment "I am overjoyed," does not enter the life of the individual as *deus ex machina.* It is preceded by long periods of dreary expectations and long barren stretches when success is absent from the circumscribed area of activity. If this were not so, the reaction to the happy event would be mere complacency: The expected outcome has materialized.

Both dreary expectations and periods when success is not forthcoming unconsciously mobilize a good dose of psychic masochism in the form of inner fears. Once psychic masochism—the unconscious pleasure-in-displeas-

*I described this phenomenon in a study entitled "Paradoxical tears—tears of happiness." (Dis. Nerv. System 13:337-338, 1952.)

ure pattern—is activated, it cannot be dismissed without discharging its accumulated and "ready to jump" store of energy. If the outcome of dreary expectations is a flat failure, the ensuing depression absorbs the masochistic discharge. But if, unexpectedly, the outcome is favorable, a new deposition is inwardly sought and found. Despite the happy event, *the beneficiary behaves as if he were bemoaning the suffering that preceded the fortunate result.*

This mechanism can be illustrated by an old gag. A passenger in a train moans audibly. His neighbor, unable to concentrate on his magazine, asks if he is in pain. The afflicted one explains that he is suffering from excruciating intestinal cramps. The neighbor, a good Samaritan, offers some pills, which are accepted. Immediate relief follows the taking of the medicine. The good Samaritan returns eagerly to his magazine, but his peace is again disturbed by a second performance of moans and groans. "Are you in pain again?" he asks. "No," is the reply, "but I'm thinking of the pain I had before." Substitute for the conscious irony of the witticism an unconscious technic and the simile fits.

One could conclude that the more pain is subsumed in the actual process of giving birth the less postpartum depression is to be expected. The conclusion is erroneous. The yardstick is not the *actual* pain and discomfort experienced but it is the *"psychic amount" prepared for the event.* If the fear was overdimensional, even a painful birth will not absorb all the expected suffering. The "leftover" will be materialized in the ensuing depression.

This depression is really a "depression because of missed masochistic opportunities," as I would call it.* This is a new and, so far, never-stressed element in depression, although the principle of discharging accumulated psychic energy (cathexis) is a basic psychoanalytic principle that views psychic phenomena as dynamic, not static.

One should not be deceived by the fact that these masochistic-tinged depressions (using as vehicle infantile repressed fears, later rationalized) are frequently cloaked in guilt because of "aggressive" thought. That "aggression" is but spurious aggression (pseudoaggression), hiding the real masochistic substratum. Then, guilt is accepted for the "lesser intrapsychic crime" (aggression). It should also be stated that guilt and psychic masochism are not identical: Punishment and guilt are precursors, and they are later changed into some *inner* pleasure—the pleasure in displeasure.

It is obvious that the clinical material presented—five cases—is not sufficient to draw on for very far-reaching conclusions. I am therefore presenting these findings in a tentative manner, and suggesting further research. If the obstetrician and general practitioner apply the preventive technic advocated, there is no danger of damaging the patient. At worst, if the physician is unsuccessful in preventing postpartum depression, he has at least given the patient something to hold onto. It is a lot better for the woman to bear in mind, after the child is born, that her depression corresponds to the discrepancy between prepared and used-up fears than for her to believe, in her depression, that her whole life is collapsing.

Personally, I am expressing the cautious conviction that the avoidance technic outlined here, although it amounts to no more than a stopgap, will be of benefit to suffering women and at the same time initiate a better understanding between psychiatrist and general practitioner, gynecologist and obstetrician.

*Further elaboration in my study, "Depression as aftereffect of missed masochistic opportunities." (Psychiat. Quart. [In press.])

Certain morbid conditions would be diagnosed more often if the genitalia were inspected routinely during examination of the premenarchal child. If obvious preliminary steps are taken and if the examiner exercises gentleness and patience and uses a few specially designed instruments, the examination is seldom difficult. In addition to discussing the technic of such an examination and the auxiliary procedures to be used, the author describes the anatomic peculiarities of the immature genitalia and abnormalities which may be encountered.

Gynecologic Examination of the Premenarchal Child

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ALTHOUGH it is true that the incidence of gynecologic troubles is less among children than it is among adolescents and adults, there is reason to believe that certain morbid conditions would be diagnosed more often if inspection of the genitalia were routinely a part of the examination of the premenarchal child. This applies particularly to the diagnosis of congenital anomalies, vulvovaginitis, labial adhesions and genital tumors.

The examination is seldom a difficult task when certain rather obvious preliminary steps are taken. The mother is told that the special instruments to be used and the method of examination will not cause the child pain, will not injure her, and will not damage the hymen. Good rapport between the examiner and his young patient is essential before any attempt at examination is made. If the child is old enough to understand, she is told that nothing will be done which will hurt her and that the examination is comparable to inspection of the throat or to having a rectal temperature taken. She is also assured that the examiner will keep his word when he promises to discontinue his efforts if what he is doing causes pain.

Patience and gentleness are always necessary, but particularly so when the child is frightened and rebellious. Usually, a capable, sympathetic assistant is more helpful during the examination than a worried mother who transmits her apprehension to her daughter. Examination by force of a terror-stricken child is unjustifiable. Attempts to do so are physically and psychically traumatic. The results of such an examination are almost always unsatisfactory, and it may make the child antagonistic to necessary gynecologic examinations in later life. It causes the mother anguish and embarrasses or aggravates the physician. Re-

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TABLE 1

INDICATIONS FOR GYNECOLOGIC EXAMINATION

Genital infection
Anomalies of the genitalia
Vaginal foreign bodies
Precocious sexual maturation
Delayed sexual maturation
Abnormalities of somatic growth
Intersex
Psychosexual problems
Tumors of the genitalia
Certain anorectal conditions and disorders of the lower part of the urinary tract
Certain systemic disorders

calcitrant children should be examined under anesthesia. Such children have been encountered rarely in my experience when time has been taken to prepare the mother and patient for what is to be done.

Indications for gynecologic examination of the premenarchal child are listed in table 1. The genitalia of all newborn female infants should be inspected at birth to exclude the presence of both congenital abnormalities and neoplasms.

The signs and symptoms which most often cause the parents to bring the child for examination are given in table 2. With the exception of bleeding from the vagina of a newborn infant, all of these conditions are indications for a gynecologic examination. Vaginal bleeding during the first week of life, due to withdrawal of maternal hormonal stimulation, stops after a few days. Its continuance for a longer period is an indication for examination, since it may be a symptom of a tumor of the vagina or uterus.

TABLE 2

SIGNS AND SYMPTOMS WHICH CAUSE PARENTS TO HAVE THE CHILD EXAMINED

Vaginal discharge
Vaginal bleeding
A dermatologic disorder of the perineum or vulva
A sore or lump on the external genitalia
Precocious development of sexual hair, the breasts and genitalia, or of any of these
Abnormal form of the external genitalia
Rectal or urinary symptoms
Pain in lower part of the abdomen
Questionable sexual molestation
Abnormal sexual behavior
Aberrant somatic growth

History

The history depends on the problem and the age of the child. It will, of course, be obtained from the mother of an infant or small child. The gentle exclusion of an excitable oversolicitous parent from the consultation room will frequently result in obtaining a more accurate story from an older girl, particularly if sexual practices are part of the problem. Time spent in obtaining the older girl's confidence will often elicit facts not known by the family. In many cases, this can be managed expeditiously without going into sociologic or psychologic matters. In others, essential facts are obtained only after prolonged and sometimes repeated conferences.

Examination

General inspection is the first step in examination. The child's habitus is noted. Cognizance is taken of obvious congenital anomalies, abnormal skeletal growth, obesity or unusual muscular development. Poor hygiene and nutritional deficiencies are sometimes etiologic factors in cases of genital disorders. Tics, misbehavior, mental retardation, precocious intelligence and disinterest are, at times, signs of endocrine disorders, intracranial lesions or psychic disturbances related to the trouble for which the child is examined.

Changes in body structure and size are encountered most frequently in cases of sexual precocity, gonadal dysgenesis, hypo-ovarianism and virilism. The last includes the changes associated with congenital adrenocortical hyperplasia, postnatal adrenocortical disorders associated with increased androgenic hormone production, the masculinizing changes associated with certain pituitary disturbances and hermaphroditism.

There are wide variations in the age at which the signs of sexual maturation first become evident. As a general rule, breast development, growth of pubic hair, and estrogen stimulation of the vaginal epithelium do not appear before a child is seven years of age. Menstruation prior to a girl's tenth birth-

day is considered abnormal. Evidence of ovarian activity should be present by the time a girl is 12 years of age. The menarche may be delayed until she is 15 years old without causing undue concern provided she has no other signs of endocrine or systemic disorders. Examination is indicated if a girl has not had her first menstrual period by the time she reaches her sixteenth birthday.

Inspection and palpation of the breasts and abdomen precede examination of the genitalia. Light palpation of the abdomen, moving slowly from one area to the other, is more informative than deep pressure. The examiner's hands must be warm. Tumors of the ovary large enough to be palpated abdominally are more likely to be mistaken for other abdominal masses in children than in adults. The ovary of the premenarchal girl normally lies high in the pelvis; this and the small size of the pelvic cavity tend to force ovarian tumors into the middle of the abdomen above the brim of the true pelvis.

Children should be permitted to sit up until time for the examination. They become apprehensive when forced to lie supine on an examining table for some time. When the examiner is ready, an infant or small child is placed in her mother's or in a nurse's lap, or on her back on the examining table. The mother, a nurse or an assistant separates the child's thighs and brings the knees upward onto the abdomen. The Sims position does nicely for the slightly older girl; her face is turned away from the examiner so that she does not see the instruments or what is being done. The knee-chest position is useful in examining the cooperative adolescent and an anesthetized child in whom a pneumoperitoneum has been induced. It is uncomfortable and frightening to small children. I do not recommend it for the premenarchal patient. The majority of older children use the stirrups attached to an ordinary gynecologic table. Adjustable shoulder braces, similar to those on an operating table, keep the patient from sliding upward. Most of them are more contented with a pillow under the head and shoulders. If the cervix cannot be found easily, as is sometimes the case in small children, the child is placed in a dorsal recumbent position with the thighs flexed on the abdomen.

The pudendal area is inspected. The perineal skin may be affected by any one of a number of dermatologic conditions ranging from irritation and inflammation, as a result of uncleanliness, to lesions which are a part of a disorder involving other body areas. Tumors of the perineum and vulva are very rare during childhood, just as are other neoplasms of the genitalia. It must not be forgotten, however, that almost all types of genital tumors affecting adults have been observed in girls less than 16 years of age, and that the presence of a neoplasm must be considered whenever a child has a chronic ulcerative lesion or a persistent mass.

The labial skin and subcutaneous tissues and the vulvar mucosa are responsive to estrogen stimulation. They lose their turgescence shortly after birth when the effect of the mother's hormones wanes. During early childhood, the labial swellings are flat, the labial skin smooth and pale, and the vulvar mucosa thin and somewhat hyperemic. Thickening, wrinkling and the darkened color of the labial integument, fullness and swelling of the labia, cornification of the vulvar mucosa, the appearance of pubic hair and other evidences of beginning sexual maturation normally occur when the child is between 7 and 10 years of age. The presence of signs of hormonal stimulation in early childhood and their absence at a later time, when they should be evident, are diagnostically significant in the many endocrinopathic problems associated with precocious or delayed growth of the sexual organs.

The clitoris is disproportionately larger during infancy than it is later in life. Its size is diagnostically important in cases of virilism or intersex. Marked enlargement is associated with an increased secretion of androgenic hormones. Clitoral hypertrophy is usually present together with gross anomalies of the genitalia in cases of congenital adrenocortical hyperplasia and true hermaphroditism. Postnatal clitoral hypertrophy without anomalies of the genitalia suggests adrenocortical hyperplasia or tumors, or pituitary disorders causing virilism. Preputial adhesions, which are common-

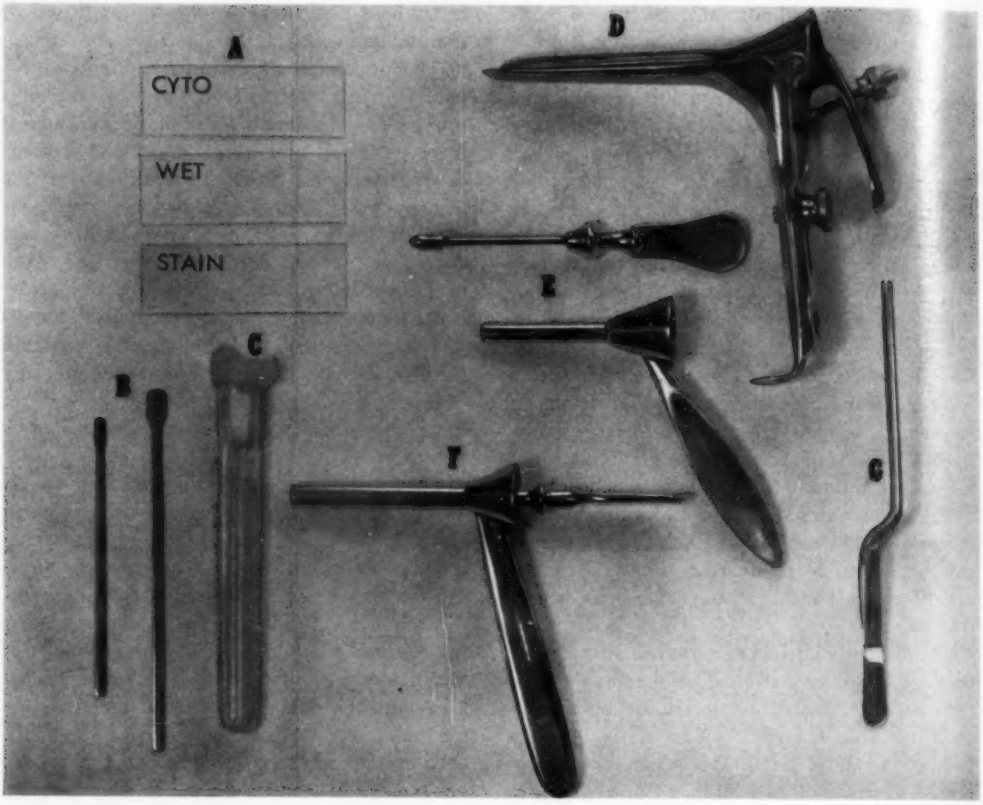

FIGURE 1. Instruments for gynecologic examination of the premenarchal child.
A. Glass slides for microscopic examination of vaginal cytosmears, wet preparations and stained smears.
B. Metal spatulas used in obtaining vaginal fluid.
C. Sterile culture tube which usually contains liquid media.
D. Author's narrow (1 cm.) long-bladed (11 cm.) modification of the Graves vaginal speculum used occasionally for examination of girls approaching the menarche.
E. Small, short (5 cm.) vaginoscope for examination of infants and young children.
F. Larger, longer (7 cm.) vaginoscope for examination of older children.
G. Long-bladed bayonet forceps for the removal of foreign bodies.
The vaginoscopes are shortened Kelly air cystoscopes.

ly seen in infants, are not significant unless inspissated smegma causes vulvar irritation and discomfort manifested by rubbing or scratching.

The vestibule, the space between the labia minora and outside the hymen, is exposed by light lateral and downward pressure on each side of the perineum. It may not be visible because of congenital anomalies or more often because of a postinflammatory adhesion between the labia minora. The latter is frequently mistaken for vaginal agenesis or an imperforate hymen. A zone of inflammation about the urethral meatus will sometimes explain dysuria in a child just as it will in a postmenopausal woman.

Vulvovaginal inflammation causing a discharge outnumbers all other gynecologic disorders in premenarchal girls. The degree of inflammation, other lesions, the cleanliness of the parts and the amount and character of the discharge are noted. A purulent or blood-

tinged serous discharge is a sign of an infection, a foreign body or a tumor. A menstrual-like flow frequently accompanies and may be the first symptom of sexual precocity.

The hymen of the normal newborn infant is a succulent, cone-shaped curtain pointing outward into the vestibule. Its folded edges hide the centrally placed opening. In early childhood, the hymen is a thin, flattened, diaphragmatic membrane. Later, as the older girl develops her own hormones, the hymen tends to regain the appearance it had during the immediate postnatal period. In infancy and childhood, the hymenal orifice will normally admit a vaginoscope having a diameter of 0.5 cm. An instrument with a diameter of 0.8 cm. can be used to examine most older, yet still premenarchal, girls. The marked differences observed in the thickness of the hymens and in the size of the openings in different children seem to represent congenital variations and are without any clinical significance. If the aperture is too small for an instrument to be passed without discomfort, vaginoscopy should not be attempted until the child is anesthetized. Persistent manipulation of the sensitive tissues without anesthesia will be traumatic and nonproductive. An imperforate or cribriform hymen will be discovered on inspection.

A nasal speculum may be used for the vaginal examination of an infant or a little girl if a vaginoscope is not available. However, a nasal speculum causes more discomfort than a vaginoscope; also, it is not long enough to permit inspection of the vaginal vault and cervix of the older child. The instruments which I use are illustrated in figure 1. After the vaginoscope has been inserted, the examiner inspects the cervix and the walls of the upper part of the vagina. The field is illuminated with a head mirror or a head lamp. The portio of the cervix is a small flattened, buttonlike or nipple-shaped projection during most of childhood. It does not assume its adult form until near the menarche. Cervical disorders are extremely rare before late adolescence. An adult-type cervix is sometimes, but not always, seen in sexually precocious youngsters. The child's vaginal canal is nondistensible and relatively narrow; it does not acquire its adult roominess and pliability until after the menarche. The healthy vaginal mucosa in early childhood is pink in color, thin, and has relatively few rugae. The reaction of the scanty vaginal fluid is neutral or alkaline. In late childhood, the ovary begins to secrete increasing amounts of estrogen, which cause thickening and cornification of the epithelium. The mucosa acquires a lighter and duller pink color, the rugae become larger, and the vaginal fluid increases in amount and has an acid reaction.

It should be pointed out at this time that there is no specific pattern for activation of the various organs stimulated by the rising hormonal titers of the premenarchal period. Somatic changes usually occur first, and are followed in sequence by growth of pubic hair, breast development, vulvovaginal epithelial thickening and cornification, and, last, by endometrial bleeding. In some children, however, any one of these phenomena may precede the others by some little time. Diagnostic problems arise when the sequence is not always followed and, also, when the first sign of maturation appears precociously. For example, there are girls who develop a heavy growth of pubic hair at six years of age without any other signs of sexual maturation or adrenocortical hyperactivity. There are others who have cyclic episodes of uterine bleeding or well-cornified vaginal epithelium when seven or eight years old without the other end organs revealing signs of hormonal stimulation.

As the vaginoscope is withdrawn the mucosa is examined. Note is taken of inflammatory reactions, discharge, ulcerative lesions or tumors. A search is made for foreign bodies. The commonest foreign bodies I encounter are bits of rolled-up ravelings of bedclothes or night clothes, or pellets of toilet tissue. Toys, erasers, beans, crayons, bobbie pins and other small objects have also been removed from children's vaginas. A foul-smelling, blood-streaked, purulent discharge is almost pathognomonic of a foreign body. Cultures, dry and wet smears, smears for cytologic examination, and preparations to be examined for parasite ova are made if indicated.

It is impossible to make a digital vaginal examination of the premenarchal girl. Rectal digital examination can be made without causing the child undue distress. Gentleness is essential. Most tumors of the lower part of the abdomen are palpable and, frequently, the normal ovaries and uterus can be outlined if the child is cooperative or anesthetized. Rectoabdominal examination is sometimes difficult because the child is resistant, the tissues are firm, and the genitalia are of small, almost fetal size. If the presence of a pelvic tumor is suspected and it is not found by rectal examination, roentgenographic examination should be performed after a pneumoperitoneum has been induced.

Auxiliary Procedures

In all cases in which there is a vulvovaginal discharge, except those in which a foreign body is present in the vagina, cultures of the discharge are made and smears are examined microscopically. In cases in which the discharge is due to the presence of a foreign body, the inflammation will disappear after the foreign body is removed. In most cases, the discharge is associated with vulvovaginitis. A sterile, warm metal spatula (figure 1), instead of a cotton-tipped applicator, is used to obtain the specimen of the discharge. The cotton-tipped applicator absorbs most of the fluid and is likely to cause discomfort when it catches on the vaginal rugae. The material is cultured for predominant organisms and for *Neisseria*. The former are tested for antibiotic sensitivity. A dry smear is made for routine examination. Fresh wet preparations are examined microscopically in the clinic or office for mycotic organisms and *Trichomonas vaginalis*. Occasionally, a wet smear obtained from an older youngster who presumably has a vaginal discharge shows that the increased amount of vaginal fluid is due to an exuberant premenarchal exfoliation of cornified epithelial cells and that few leukocytes but no fungi or trichomonads are present. In other words, she has an excessive amount of normal vaginal fluid. Vaginal infections due to *Candida albicans* are not uncommon in children, and their presence should be suspected, particularly if a vulvovaginitis appears after a child has received antibiotics. Vaginal trichomoniasis is rare before the menarche.

Vaginal smears, material from the perineal skin or stool specimens, or all three should be examined for pinworm ova in all cases of intractable chronic vulvovaginitis and perineal pruritus in little girls. The adult worm will occasionally enter the vagina and deposit ova. Cultures of the discharge in such cases will almost invariably yield bacteria of the coliform group.

In all cases in which there is a history of abnormal bleeding or an unexplained vaginal discharge, smears are obtained and prepared for cytologic examination. These smears are stained by the method of Papanicolaou or Schorr. Examination of such smears serves a twofold purpose: (1) It furnishes a relative indication of ovarian activity, and (2) it may indicate the presence of a neoplasm. A metal spatula is used to obtain the material for the smear. Wooden applicators should not be used because they cause pain and absorb the fluid. Examination of the vaginal cells of a child who is less than seven years old normally reveals little if any evidence of estrogen stimulation. A smear obtained from a girl in early childhood is significant if it contains cornified epithelial cells. Such cells are an indication of constitutional sexual precocity, of an estrogen-producing ovarian tumor, of ovarian stimulation by a disturbance of the cerebral-hypothalamic-hypophysial apparatus, of the abnormal production of estrogen by the adrenal cortex, or of the use of hormonal therapy.

Hormonal assay is used if indicated. Estrogen titration seldom is necessary. Precocious isosexual development and the presence of numerous cornified cells in the smear are indications of the excessive production of estrogen. Estrogen titration will not distinguish estrogen-producing ovarian tumors from constitutional sexual precocity. Masculinization, intersexual genital anomalies and increased excretion of 17-ketosteroids are associated with congenital adrenocortical hyperplasia. An increased excretion of 17-ketosteroids, masculinization, and hypertrophy of the clitoris associated with morphologically normal female

genitalia are signs of extragenital androgenic hormone secretion, and usually are due to adrenocortical hyperplasia or tumors. A teratomatous chorio-epithelioma of the ovary may or may not produce enough chorionic gonadotropin to be detected by a biologic test.

Roentgenographic examination is used to demonstrate the presence of a radiopaque foreign body in the vagina, to estimate the bone age, to reveal the presence of a suspected abdominal tumor, to distinguish adrenal tumors from genital tumors, to demonstrate the size and shape of the internal genitalia after a pneumoperitoneum has been induced, and to outline the contour of the vaginal canal following the intravaginal instillation of a radiopaque fluid.

Many materials, including vegetative matter, cloth and some plastics, are not radiopaque. Failure to demonstrate the presence of a foreign body roentgenographically does not preclude one being in the vagina. Advanced bone age, the result of increased estrogen production, is one of the stigmata of constitutional sexual precocity and of hormone-producing tumors of the ovary. It also occurs with adrenocortical and other extragenital disorders causing accelerated skeletal growth. Abdominal tumors may or may not be revealed by the use of scout films. The commonest ovarian neoplasm in childhood, a benign cystic teratoma or dermoid, usually contains calcareous material which will be seen on a scout film. Roentgenographic examination after the intra-abdominal injection of carbon dioxide gas, i.e., induction of a pneumoperitoneum, is an essential diagnostic procedure when a child is believed to have a tumor of the internal genitalia, in cases of sexual precocity or delayed development, gonadal dysgenesis, pseudohermaphroditism and other congenital anomalies of the genitalia. Vaginograms are used in the study of intersex problems and are helpful in determining the size of the vagina above a pinpoint-sized introitus opening onto a distorted perineum or into a urogenital sinuslike cavity.

Identification of chromosomal sex by study of chromosomal patterns in sections of skin and buccal smears, and neutrophilic leukocyte nuclear shapes are used in cases of gonadal dysgenesis and intersex problems. The tests are sometimes helpful, but are not as yet specific enough to take the place of gonadal biopsy. At the present time, gonadal biopsy is the only method of definitively identifying the sex of the sexually indeterminate child.

Comment

I would like to emphasize that a gynecologic examination need be neither physically nor psychically traumatic to the premenarchal child. The technic of the examination itself is very easy when the examiner exercises gentleness and patience and uses a few simple, specially designed instruments. The primary purpose of this presentation is to point out the indications for examination, the salient points in its performance, and the value of certain auxiliary procedures. Several other things have been mentioned, more or less indirectly, which are as important as the technical aspects of the examination. The examiner should be acquainted with the anatomic and physiologic peculiarities of the immature genitalia. He should also be able to correlate what he sees in his young patient with the embryonic and fetal developmental changes which have gone before and the adult status which will come later. Examination is and, of course, always should be a prelude to treatment. Management of a little girl's genital trouble, whether it is a vaginal discharge or an ovarian cyst, in most instances is based on a knowledge of gynecologic pathology and of the principles of gynecologic treatment.

Studies of 182 patients revealed that the microflora found in normal ears differs significantly from that found in the ears of patients with otitis externa or otitis media. The authors determined the bacterial sensitivity to common antibiotics and, on the basis of the studies, recommend a combination of polymyxin B, neomycin and bacitracin for treating external otitis and chronic otitis media. The latter condition often does not respond to antibiotic therapy, and in some cases adenoidectomy or mastoidectomy is suggested as a better treatment.

The Microflora and the Treatment of External Otitis and Otitis Media

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TREATMENT of infections of the external ear canal and of the middle ear is difficult for many reasons. In otitis media there is inadequate drainage of the tympanic cavity. In external otitis the edema of the ear canal causes pain which often makes adequate examination impossible. The bacteria causing external otitis and otitis media are extremely varied. No single medication is effective in all cases.

Other investigators[1-4] have described the bacterial flora of the normal ear canal and the organisms found in infections of the ear. We have repeated these studies to determine whether the normal and pathogenic flora in Ohio differ significantly from those described in previous studies. We have determined the bacterial sensitivity to common antibiotic drugs using the paper disk method. On the basis of these studies we believe it is possible to select a combination of antibiotic drugs for em-

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TABLE 1

MICROFLORA OF NORMAL EARS, OTITIS EXTERNA AND OTITIS MEDIA

ORGANISM	NORMAL EARS (50 SUBJECTS)		OTITIS EXTERNA (66 PATIENTS)		OTITIS MEDIA (66 PATIENTS)	
	Number	*Per Cent*	*Number*	*Per Cent*	*Number*	*Per Cent*
Staphylococcus (coagulase-positive)	0		18	27.3	12	18.2
Staphylococcus (coagulase-negative)	50	100	20	30.3	23	34.8
Diphtheroids	13	26	1	1.5	1	1.5
Anaerobic *Streptococcus*	2	4	0		1	1.5
Chromobacterium	2	4	0		0	
Streptomyces	1	2	0		0	
Ps. aeruginosa	0		30	45.5	21	31.8
Alpha *Streptococcus*	0		18	27.3	17	25.8
Beta *Streptococcus*	0		2	3	2	3
Gamma *Streptococcus*	0		6	9.1	4	6
Diplococcus pneumoniae	0		0		3	4.5
A. aerogenes	0		3	4.5	7	10.6
Klebsiella pneumoniae	0		1	1.5	1	1.5
Esch. coli	0		6	9.1	10	15
Candida	0		1	1.5	2	3
Aspergillus	0		2	3	0	
Bacillus subtilis	2	4	0		1	1.5
Alcaligenes faecalis	0		1	1.5	3	4.5
P. vulgaris	0		9	13.6	20	30.3

pirical use as ear drops or ointment in the treatment of external otitis and to a lesser extent in the treatment of chronic otitis media.

Method and Material

Two groups of subjects were selected, consisting of 132 patients with otitis media or otitis externa and 50 subjects without infection of the ear. Using aseptic technics, ear swabs were placed in thioglycollate broth. The tubes were incubated at 37° C. From the first growth to appear in the broth, a smear was made and a brain-heart infusion blood agar plate was streaked. The pure cultures obtained were identified by standard biochemical tests. Then, using coagulase tests, the potential pathogenicity of the staphylococci was determined.[5] Absence of growth in thioglycollate broth after seven days was considered a negative result. Bacteria isolated from blood agar plates were streaked heavily on other blood agar plates. Antibiotic and FURACIN® disks were placed 2 cm. apart in this medium. The plates were examined for zones of inhibition after 6 and 24 hours and the sensitivity was determined by the presence or absence of a clear zone around the disks.

Findings

Table 1 shows the difference between the microflora found in normal ears and the microflora found in infected ears. The organisms found most often in normal ears were *Staphylococcus albus* (coagulase-negative) and diphtheroids. In contrast to the relatively few genera of bacteria in normal ears, a large number of different bacteria were isolated from the infected ears. Staphylococci, streptococci and gram-negative rods predominated. Of the gram-negative organisms the most frequently found were *Pseudomonas*, *Proteus*, *Aerobacter* and *Escherichia*.

Seventy per cent of the patients with ear disease had a mixed bacterial flora. In other words, a single organism was isolated in only 30 per cent. It was common to find gram-positive cocci in association with gram-negative rods. Only 3 per cent of the infections were due to fungi, a somewhat lower incidence of fungous infections than that reported in other studies.

Table 2 presents the antibiotic sensitivity of the commonly encountered organisms. All strains of *Pseudomonas* and the coli-aerogenes

TABLE 2

ANTIBIOTIC SENSITIVITY OF BACTERIAL ISOLATES FROM OTITIS EXTERNA AND OTITIS MEDIA

DRUG	CONCENTRATION	SUSCEPTIBILITY OF BACTERIAL ISOLATES									
		Ps. aeruginosa		*P. vulgaris*		*Staphylococcus*		*Streptococcus*		*Coli-aerogenes*	
AUREOMYCIN®	30 mcg.	17/54*	31.5†	2/22	9.1	36/57	63.2	21/22	95.5	24/25	96
	10 mcg.	11/54	20.4	2/22	9.1	31/57	54.4	17/22	77.3	24/25	96
	5 mcg.	6/54	11.1	2/22	9.1	29/57	50.9	16/22	72.7	23/25	92
Bacitracin	20 units	0/57		0/17		45/46	97.8	16/17	94.1	0/17	
	10 units	0/57		0/17		44/46	95.7	16/17	94.1	0/17	
	2 units	0/57		0/17		23/46	50	16/17	94.1	0/17	
CHLOROMYCETIN®	30 mcg.	15/54	27.8	12/21	81	41/50	82	21/21	100	23/23	100
	10 mcg.	4/54	7.4	14/21	66.7	38/50	76	21/21	100	22/23	95.7
	5 mcg.	0/54		9/21	42.9	37/50	74	21/21	100	22/23	95.7
Dihydrostreptomycin	100 mcg.	46/54	85.2	17/22	77.3	30/55	54.5	9/22	40.9	23/25	92
	10 mcg.	23/54	42.6	12/22	54.5	27/55	49.1	4/22	18.2	21/25	84
	2 mcg.	2/54	3.7	5/22	22.7	20/55	36.4	2/22	9.1	8/25	32
Penicillin	10 units	0/57		1/23	4.3	28/60	46.7	20/22	90.9	0/25	
	5 units	0/57		1/23	4.3	24/60	40	20/22	90.9	0/25	
	2 units	0/57		0/23		22/60	36.7	20/22	90.9	0/25	
Polymyxin B	30 mcg.	57/57	100	1/23	4.3	3/60	5	1/22	4.5	25/25	100
	10 mcg.	57/57	100	0/23		0/60		0/22		25/25	100
	5 mcg.	36/57	63.2	0/23		0/60		0/22		23/25	92
TERRAMYCIN®	30 mcg.	41/54	75.9	3/23	13	32/58	55.2	18/22	81.8	24/25	96
	10 mcg.	21/54	38.9	2/23	8.7	30/58	51.7	17/22	77.3	24/25	96
	5 mcg.	10/54	18.5	1/23	4.3	30/58	51.7	17/22	77.3	24/25	96
Neomycin	30 mcg.	48/57	84.2	19/23	82.6	53/56	94.6	3/23	13	25/25	100
	10 mcg.	39/57	68.4	16/23	69.6	53/56	94.6	1/23	4.3	22/25	88
	5 mcg.	16/57	28.1	11/23	47.8	51/56	91.1	1/23	4.3	22/25	88
Tetracycline	30 mcg.	32/54	59.3	5/23	21.7	37/57	64.9	21/22	95.5	24/25	96
	10 mcg.	12/54	22.2	4/23	17.4	30/57	52.6	17/22	77.3	23/25	92
	5 mcg.	7/54	13	3/23	13	30/57	52.6	17/22	77.3	23/25	92
Erythromycin	15 mcg.	0/57		0/23		49/59	83.1	23/23	100	0/25	
	5 mcg.	0/57		0/23		49/59	83.1	23/23	100	0/25	
	2 mcg.	0/57		0/23		49/59	83.1	23/23	100	0/25	
ALBAMYCIN®	100 mcg.	0/43		14/17	82.4	42/42	100	20/20	100	7/14	50
	30 mcg.	0/43		11/17	64.7	42/42	100	20/20	100	3/14	21.4
	5 mcg.	0/43		5/17	29.4	42/42	100	18/20	90	1/14	7.1
FURACIN®	100 mcg.	0/51		18/20	90	49/49	100	18/18	100	19/19	100

*Number of strains sensitive/number of strains tested.

†Per cent of strains susceptible.

groups tested were sensitive to polymyxin B. All strains of the streptococci were sensitive to erythromycin, CHLOROMYCETIN® and also to ALBAMYCIN® in higher concentrations. Furacin was very effective against staphylococci, streptococci and the coli-aerogenes group but ineffective against *Pseudomonas*.

Choice of Therapy

Antibiotic treatment of infections of the external ear and middle ear is difficult. Unlike infections of the eye,[6] in which commonly one pathogen is isolated, cultures of ear infections usually show two or more pathogenic organisms. The findings of our study closely parallel those of similar surveys.[1,3] Since no antibiotic is effective against all the organisms, the clinician usually must decide empirically which antibiotic drug to use.

Chronic otitis media often fails to respond to any type of antibiotic therapy. Sometimes the infection is too deeply established, or the antibiotic in the form of drops cannot get into the middle ear in effective amounts. In other cases a surgical procedure such as adenoidectomy or mastoidectomy is better treatment than either local or systemic antibiotics. Many instances of external otitis are due to a dermatosis. In these and other cases, meticulous cleansing of the ear canal is more essential to recovery than is the use of antibiotic preparations.

If antibiotic treatment is indicated, it is helpful to know which drugs are most likely to be effective. As a result of our in vivo studies and from clinical observation of the patients with ear infections included in our survey, we believe a preparation containing polymyxin B, neomycin and bacitracin (gramicidin in case of drops) would be the most effective topical medication for empirical use in ear infections. These antibiotics have the following advantages: (1) Combined they form a preparation effective against gram-positive and gram-negative bacteria. (2) They are seldom used systemically, and therefore sensitization to broad-spectrum antibiotics such as tetracycline is avoided. (3) They have a comparatively low sensitizing index.[7]

Conclusions

1. The microflora found in normal ears differs significantly from the microflora found in the ears of patients with otitis externa and otitis media.

2. A combination of polymyxin B, neomycin and bacitracin is recommended in treatment of external otitis and chronic otitis media. Furacin is very effective against infections due to gram-positive cocci.

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Inadequate hospital facilities and consultation services in rural communities, evidenced by high infant and maternal mortality, constitute one of the most pressing problems in American medicine. Solution of this problem requires the cooperation of the medical profession and the local community, as exemplified by Hunterdon Medical Center, Flemington, New Jersey. The author describes in detail the Center's facilities for improving private and hospital practice and for providing opportunities for postgraduate teaching and discussion.

Obstetrics in a Rural Community

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My interest in the problem of providing adequate medical care in the rural areas of our country was first stimulated by my experiences as a trained obstetrician and gynecologist practicing in a region which was chiefly rural, at least as far as the practice of medicine was concerned. It was evident to me that most of the maternal and fetal deaths could have been avoided had adequate provisions been made for proper hospital care and the ready availability of consultation services. In discussing this concern of mine with others and in studying national figures, as well as by reading commentaries by others interested in this field, I soon found that I was not alone in my concern about this problem. As a matter of fact, I was impressed by the feeling that many interested people felt that this was perhaps the most pressing problem in American medicine. It also became evident that any attempted solution of the problem would be complicated by the facts that these rural and semirural areas have less concentrations of wealth, hospitals are few indeed, the general physician is often at a premium, and the specialist is practically unknown.

Figure 1 shows the distribution of general physicians and specialists, according to size of community, and emphasizes the dearth of specialists in communities of 5000 and under as contrasted with the unusually high percentage of general physicians. Unfortunately, this figure shows no breakdown for the various specialties, but certainly the proportionate concentration of physicians practicing obstetrics and gynecology is no greater than that for all specialists plotted in this figure, and is quite probably less.

Table 1 dramatically emphasizes the difference in infant and maternal mortality between

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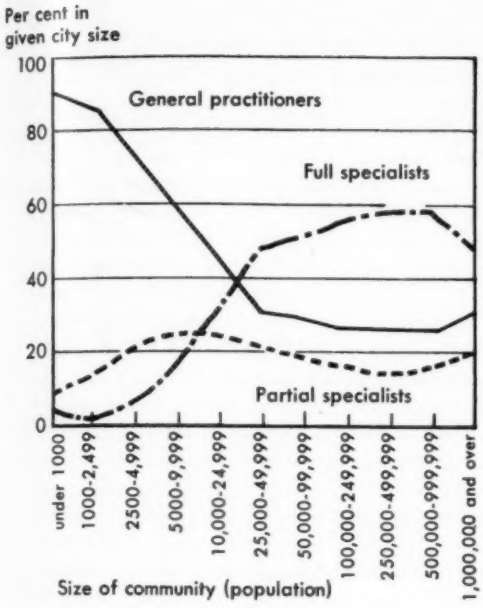

FIGURE 1. Distribution of general physicians and specialists according to size of communities.

Based on a survey of the medical professions made in 1950 by the U. S. Department of Commerce and the American Medical Association.

metropolitan and rural areas. In the rural areas, the maternal mortality is more than twice as great as in the metropolitan areas, and, while the proportionate infant mortality rate is somewhat less, it is still significantly higher than in metropolitan areas.

There is little doubt in my mind that the reason why more physicians do not enter practice in rural and semirural communities is the absence of facilities necessary to practice good medicine and thus the absence of the stimulus and opportunity for continuing postgraduate medical education. In the absence of these necessary tools for the practice of modern medicine, the problem of medical care in many areas, both rural and semirural, will undoubtedly remain acute and urgent. It is only reasonable to assume that, after eight years of academic study and from one to five years of hospital training, the young physician will react poorly to the suggestion that he enter the practice of medicine in an area in which there is no possibility of applying the knowledge which he has acquired as a medical student, intern and resident. Therefore, if the problem of rural medical care is to be solved, the general physician as well as the specialist must be provided with an environment which will permit him to practice and give the standard of medical care which he has undoubtedly been taught to give.

The responsibility for the solution of this problem rests largely with the medical profession supported by the efforts of the local communities. Any plan to provide adequate and comprehensive medical care must result from the combined efforts of all key elements in a given community. These include the prominent lay members, the general physicians in the area as represented by the county medical society, possibly any specialists if they are present, and finally, if possible, the cooperation of a university medical center if one is present within a reasonable distance.

The Hunterdon Medical Center, of Flemington, New Jersey, is an example of the combined efforts of the groups mentioned to provide adequate medical care for a designated rural population of 45,000 in Hunterdon County. In this particular instance, the impetus for the Hunterdon Medical Center project or experiment was almost entirely "grass roots" in origin, coming from a group of community-minded citizens who recognized the urgent need for complete medical care in their area. It is interesting to note that this county was unique in that it had no hospital; nor were any specialists practicing within its geographic limits, and thus it served as an ideal location for such an exploration into this new concept of providing medical care. The newness of the concept lay merely in the fact that several recognized methods of medical practice were brought together by mutual consent of physicians having proper respect for each other's domain, for the purpose of providing a maximal standard of medical care for the people of the community.

The Hunterdon Medical Center concept recognizes an obvious fact, namely, that responsibility for the provision of medical care in rural areas rests on the general physician at

TABLE 1

INFANT AND MATERNAL MORTALITY IN METROPOLITAN, ADJACENT AND ISOLATED COUNTIES*

County group†	*Infant deaths per 1000 live births*	*Maternal deaths per 10,000 live births*
	AVERAGE RATE, UNITED STATES, 1948-1952	
United States	29.8	8.6
Metropolitan counties	27.1	6.5
Greater	25.2	6.2
Lesser	28.9	6.7
Adjacent counties	31.1	9.6
Isolated counties	34.5	12.2
Semirural	34.8	11.7
Rural	33.6	14.1
	RATIO TO GREATER METROPOLITAN RATE	
Greater metropolitan counties	100	100
Lesser metropolitan counties	115	108
Adjacent counties	123	155
Isolated counties	137	197
Semirural	138	189
Rural	133	227

*According to the National Office of Vital Statistics.

†The classification of counties is based on the 1950 census. Metropolitan counties include those with cities of 1,000,000 or more population (greater) and with cities of 50,000 to less than 1,000,000 population (lesser); adjacent counties have no city of 50,000 or more and border on or have ready access to metropolitan counties. All other counties are classified as isolated from metropolitan counties. Isolated counties include those with no urban places as large as 2500 (rural) and those with larger urban places but less than 50,000 population (semirural).

the present time, and there is no indication that present methods in the field of medical education will change this in the foreseeable future. Therefore, it is the intention of this experiment to provide the physician with a medical environment which will stimulate him to improve the quality of both private office and hospital practice. To achieve this he is given active staff status at the Medical Center if he is a practicing physician in Hunterdon County and is a member of the county medical society. He has a continuing obligation to the patient after his admission to the center, and he takes an active part in discussions concerning treatment. He thus maintains his contact with the patient and his family, writes orders, scrubs to assist in surgical procedures, if he so desires, and thus shares responsibility with the specialist on the staff for the selection and application of the best in modern therapy. He attends medical and pediatric patients and makes uncomplicated obstetric deliveries. The responsibility for normal obstetric practice is his, the role of the director being almost entirely advisory and, as the occasion requires, supervisory. A special interest by the director of the department is manifested in prenatal care, recognizing that this period of pregnancy is perhaps the most important of the entire gestational period. Some idea of the type of the prenatal care given is obtained by making a copy of the office prenatal record, a necessary requisite for a completed obstetric chart.

It may be readily seen that the arrangement described provides many and frequent opportunities for postgraduate teaching and informal discussions. The occasions for such instructions are frequent in the field of obstetrics and gynecology, as well as in the other medical disciplines. The informal or "curbstone" consultation as a medium for providing frequent opportunities for a continuing medical education is a most effective method

of keeping the general physician currently informed of advances in medicine.

The labor room is especially adaptable for this type of conference, since it is the responsibility of the director of service to follow patients in labor when deemed necessary. Thus both minor and major complications frequently are noted at the time of such rounds, and an informal review of the problem is made at that time for the benefit of the general physician, house staff and medical student. The constitution and bylaws as set up by the advisory board of the Medical Center specifically define the duties of the director of service, among which is the responsibility for the care and welfare of all patients in his department, whether specifically on his service or not. Daily rounds are made, and, while the authority of the attending general physician is not superseded, suggestions as to the proper handling of the problem may be made in the progress notes or again by informal discussion as the occasion presents itself. The latter assigned duties of the director of service have culminated in a somewhat remarkable contrast in the methods of obstetric practice, when compared with a similar role I held in private practice as Chief of Service in a general hospital located in a lesser metropolitan community. At Hunterdon, where the environment literally seethes with mutual cooperation, the general physician very readily and promptly asks for advice if he suspects a complication, with the result that a request for consultation after attempted delivery has become a rarity indeed. This is in direct contrast to previous experiences where the great majority of requests for help and advice were not made until some type of interference had been made, often with tragic consequences.

I might interpose here that the gynecologic field is especially rich with opportunities for mutual cooperation as well as for teaching. Here again, it is often on an informal basis or by means of a written report sent to the general physician following referral of a patient for consultation. It may be noted that no patients are seen by the specialists at the Medical Center unless they are referred by the general physician. Since a large proportion of gynecologic practice is office gynecology, the general physician sees a considerable number of these patients in his office each day. For instance, problems involving the use of hormones and proper therapy for the several vaginal affections are frequently discussed in the light of findings in referred patients when deemed pertinent. All aspects, such as physiology, pathology and anatomy, are discussed when they are applicable.

It has been interesting that pharmaceutical representatives have noticed the local influence of the advice of the directors of service on the general physician and, therefore, they usually present a new product to the director in order to get his reaction to it before detailing the general physician in the community.

In addition to this informal approach to medical education, the usual more formal conferences, both departmental and general staff, are held at regular intervals. Weekly staff and departmental conferences are held on most services. These are participated in by general physicians as well as by the specialists, and are attended by house staff members and students. Hence, all physicians, frequently and constantly, are exposed to teaching at one time or another and in one form or another, and their knowledge is thus improved, if only by the phenomenon of osmosis.

Graduate medical education is a constant and continuing process at the Hunterdon Medical Center. That this happy relationship has resulted in the provision of a high standard of care in all fields of medicine in the community goes without saying. This is readily evident when one studies the statistics of several clinical departments for a period of approximately three and a half years, namely, July 3, 1953 to December 31, 1956, inclusive.

During this period, there were 2,279 obstetric deliveries. Of these, delivery was made by the director of service in 271 cases, including the 56 cases in which cesarean section was performed, all cases in which delivery was made with mid forceps, and a number of cases in which the patients were referred by general physicians because of some problem, often psychosomatic in nature. The latter were usually normal cases.

Spontaneous delivery occurred in 1,695 of the entire group of 2,279 cases. Low forceps was used in 409 cases; breech delivery was made in 39 cases. An assist breech delivery was made in 33 of the 39 cases; delivery was made by manual decomposition in six cases.

As previously stated, delivery was made by cesarean section in 56 (2.5 per cent) of the entire group of 2,279 cases. In 23 of these 56 cases, the cesarean section was performed because of a uterine scar resulting from a previous cesarean section.

Episiotomy was performed in 1,132 (50 per cent) of the cases. Lacerations occurred in 334 cases. The laceration was of the first degree in 256 cases, of the second degree in 76 cases, and of the third degree in two cases. In these two cases, the classification of the laceration was questionable since the sphincter was not completely divided.

So-called morbidity occurred in 66 cases (2.9 per cent). In 21 of these cases, the morbidity was of an undetermined nature. Perinatal death occurred in 25 cases, and stillbirth occurred in 21 cases. Thus the perinatal mortality rate was 2.01 per cent.

The only blight on this unusual record was two maternal deaths, which occurred within a week of each other during the third month of operation of the Medical Center. The first of these deaths occurred in a case of pheochromocytoma. The presence of this tumor was not suspected at the time of labor. A crisis occurred after a normal delivery, and the diagnosis was not made until necropsy was done. This case was reported elsewhere in the literature. The other death was due to postpartum hemorrhage in a multipara. When the patient was referred to the Medical Center from another area, she was practically exsanguinated. The diagnosis was total placenta praevia.

I think it is evident that any department of obstetrics could well be proud of these statistics, and I think we can be doubly proud of them since the persons responsible are general physicians given the opportunity to practice the type of obstetrics which they all want to practice; that is, in an atmosphere and environment in which the care of the patient is not compromised under any circumstances, and in which all disciplines in medicine concentrate and cooperate in a mutual effort to achieve this end.

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Scientific Exhibit

Hypercortisonism

IN PATIENTS WITH RHEUMATOID ARTHRITIS

CHARLES H. SLOCUMB, HOWARD F. POLLEY,
L. EMMERSON WARD, JOHN G. MAYNE
AND ARTHUR H. BULBULIAN

Mayo Clinic and Mayo Foundation, Rochester, Minnesota

This exhibit was presented initially at the 1957 meeting of the American Medical Association in New York City.

Hypercortisonism in Patients With Rheumatoid Arthritis

Hypercortisonism is usually recognized by the general effects of Cushing's syndrome. These general effects, illustrated to the right, may occur in any person who has excesses of endogenous or exogenous cortisonelike steroids or corticotropin.

However, in patients with rheumatoid arthritis, certain additional special effects also may appear. These special effects, when they do appear, may be mistaken for a flare of rheumatoid arthritis and erroneously treated by increasing the dose of hormone, thus prolonging the hypercortisonism.

The characteristic early signs of these special effects of hypercortisonism are illustrated on pages 188, 189 and 190.

General Effects of Hypercortisonism

Supraclavicular and cervicodorsal fat pads

Rounding of the face and hypertrichosis

Ecchymoses

Increased articular damage from overuse of joint

Peptic ulcer

Osteoporosis and compression fractures of the spine

Special Effects of Hypercortisonism

I. Muscular and Joint Aching*

1 P.M.

3 P.M.

5 P.M.

Cyclic Occurrence of These Symptoms Is Characteristic

At 1 P.M. The patient's joints as well as muscles are tender to pressure. This is associated with fatigue, exhaustion and emotional instability.

At 3 P.M. After rest, sleep and a dose of prednisone only minimal tenderness of the joints is present; the patient is less fatigued and is more stable emotionally.

At 5 P.M. The patient has tenderness of muscles and joints; touch-me-not reaction recurs in a short time when she becomes fatigued from activity.

*Due to hypercortisonism from 5 mg. of prednisone given daily at 6 A.M., 2 P.M. and 10 P.M.

II. Emotional Instability*

9 A.M.

1 P.M.

3 P.M.

Cyclic Occurrence of These Symptoms Is Characteristic

At 9 A.M. After a night's rest the patient has a restless drive to get things done and has only minimal discomfort.

At 1 P.M. She is now emotionally unstable and cries "without anything to cry about" while trying to get into bed. She also complains of fatigue and aching.

At 3 P.M. After a two hour rest, with sleep, the patient has temporarily regained energy and a feeling of well-being.

*Due to hypercortisonism from 5 mg. of prednisone given daily at 6 A.M., 2 P.M. and 10 P.M.

III. Fatigability*

1 P.M.

3 P.M.

7 P.M.

Cyclic Occurrence of These Symptoms Is Characteristic

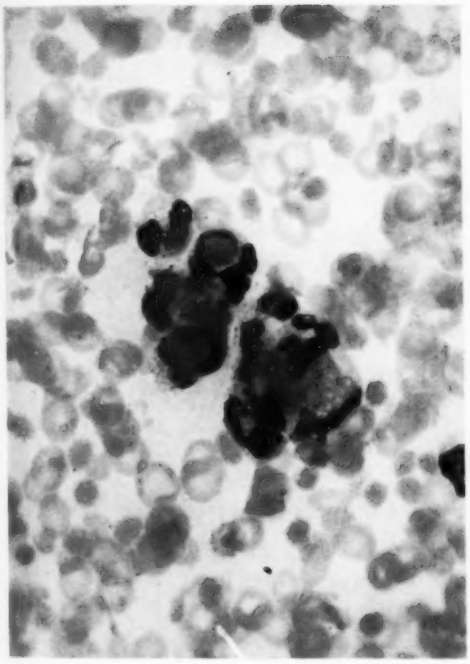
At 1 P.M. The patient is too tired and achy to get undressed. Fatigue, subjective weakness and aching appeared while she prepared a meal.

At 3 P.M. Fatigue and aching are now relieved by rest with sleep. She is ready for a visit with a friend.

At 7 P.M. By evening the patient is so fatigued that she must rest before she can finish undressing for bed.

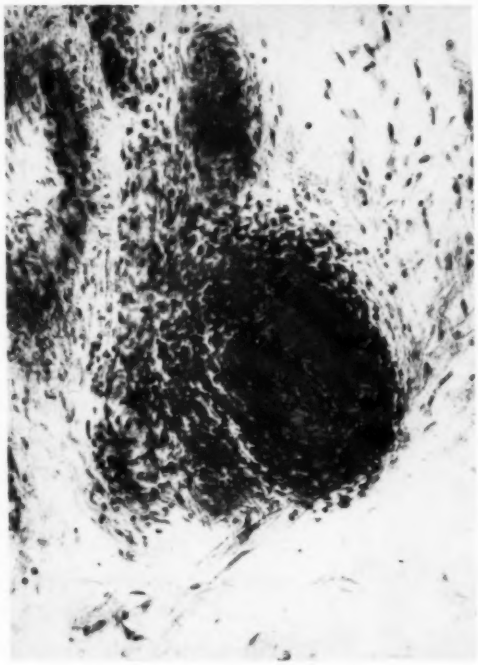
*Due to hypercortisonism from 5 mg. of prednisone given daily at 6 A.M., 2 P.M. and 10 P.M.

If Hypercortisonism Is Allowed to Continue Serious Mesenchymal Reactions Simulating Lupus Erythematosus or Periarteritis Nodosa May Develop



Lupus Erythematosus

L.E. cells resulting from hypercortisonism in a patient with rheumatoid arthritis.



Periarteritis Nodosa

Panarteritis resulting from hypercortisonism in a patient with rheumatoid arthritis.

The Reactions of Lupus Erythematosus That May Occur in Patients With Rheumatoid Arthritis and Chronic Hypercortisonism

Of 128 patients with rheumatoid arthritis and hypercortisonism, 14 per cent had positive results of L.E. clot tests.

In contrast, only 5 per cent of 166 rheumatoid patients treated with cortisonelike steroids but not having hypercortisonism and only 5 per cent of 105 rheumatoid patients who did not receive hormones had positive results from such tests.

Other signs of a lupuslike reaction, including leukopenia, albuminuria, phlebitis, ecchymoses, encephalopathy and transfusion reactions, occurred two to five times more frequently in rheumatoid patients with hypercortisonism than in rheumatoid patients without hypercortisonism.

These Reactions of Lupus Erythematosus if Recognized Early and Treated Appropriately Will Generally Subside

The Reactions of Periarteritis Nodosa That May Occur in Patients With Rheumatoid Arthritis and Chronic Hypercortisonism

Four of 14 patients with rheumatoid arthritis and hypercortisonism had evidence of diffuse periarteritis nodosa at necropsy.

In contrast, diffuse periarteritis nodosa was not found at necropsy in the 38 patients with rheumatoid arthritis not treated with cortisonelike steroids or corticotropin.

Other signs of a periarteritislike reaction, including "mononeuritis multiplex," leukocytosis, fever, nephritis and arterial occlusions, have been observed more frequently in patients with rheumatoid arthritis and hypercortisonism than in rheumatoid patients without hypercortisonism.

These Reactions of Periarteritis Nodosa if Recognized Early and Treated Appropriately Will Generally Subside

Prevention of Hypercortisonism Depends on Avoidance of Excessive Doses of Cortisonelike Steroids or Corticotropin

1. Use doses of hormones within the limits of anticipated tolerance, even though rheumatoid symptoms may not be completely relieved.
2. Employ hormones only if needed and as a supplement to physical therapy, adequate rest, salicylates, splints, corrective shoes and other appropriate treatment. Avoid abuse of involved joints.
3. Determine doses according to the patient's age, sex and tolerance; postmenopausal women are particularly susceptible to hypercortisonism.
4. Keep daily doses generally less than the following amounts both at the start of and during prolonged hormonal treatment.

	CORTISONE *(mg.)*	HYDROCORTISONE *(mg.)*	PREDNISONE *(mg.)*
Postmenopausal women	30	25	5
Younger women	40	35	7
Men	50	45	9

A program for use of cortisone for a man to avoid hypercortisonism. Changes in daily dose of 2.5 to 5 mg. with patient's progress.

5. Avoid overdosage for flares:
   a. For minor flares, use more intensive rest, physical therapy and protection of joints.
   b. For major flares, give more hormone briefly and continue other therapy intensively until dose of hormone can be reduced.
   c. For synovitis in one or a few joints, give hydrocortisone intra-articularly if needed rather than increase systemic doses.

Treatment of Hypercortisonism Depends on Successful Reduction of Doses of Cortisonelike Steroids or Corticotropin

1. Reduction of doses must be gradual.
    a. Administer doses regularly every six or eight hours.
    b. Use small decrements: 0.5 to 1.0 mg. of prednisone or 2.5 to 5.0 mg. of cortisone in a day.
    c. Allow sufficient time (days or weeks) between each decrement for symptomatic adjustment to smaller dose.
    d. Continue reduction of doses to disappearance of hypercortisonism; discontinue hormonal therapy, at least temporarily, when possible.
    e. For excessive reaction to reduction, return temporarily to previous dose and reduce more gradually thereafter.
2. Extra rest is essential.
    a. Frequent daytime rest.
    b. Extra hours of sleep.
    c. Avoidance of physical and mental fatigue.
3. Additional measures are helpful.
    a. Obtain patient's cooperation and understanding of the condition.
    b. Give analgesics, such as salicylates, in optimal doses.
    c. Use mild sedatives and tranquilizers as needed.
    d. Use physical therapy to maintain as much articular function as condition permits without accentuating fatigue.

Treatment of Hypercortisonism Is More Difficult Than Its Prevention

The Diagnostic Use of Radioactive Isotopes

4. NEWER DIAGNOSTIC PROCEDURES USING RADIOISOTOPES

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MOST diagnostic radioisotope laboratories confine their routine work to evaluation of thyroidal function with radioiodine, measurement of plasmatic volume with radioiodinated human albumin, quantitation of the absorption of labeled vitamin B_{12}, and perhaps assessment of erythrocytic survival with radiochromium.

A number of other procedures have been devised, one of which (use of radioiron in the study of the erythrocytic cycle) already has been described. Some tests have too limited usefulness, some involve too complicated instrumentation, and some require too tedious calculation to become universally applied. Still other procedures are too new to have received careful evaluation.

Certain of the more interesting or potentially useful technics will be described in this section.

Localization of Tumors

Perhaps more effort has been devoted to localization of superficial and deep tumors by means of radioisotopes than to all other diagnostic radioisotopic tests combined. The obvious conclusion is that the methods as yet are none too satisfactory.

It was recognized early that radiophosphorus (P^{32}) tends to concentrate in any malignant tissue. This probably is related to the rapid turnover of phosphorus in the nucleoproteins of cells with increased mitotic activity. Unfortunately, P^{32} emits only beta rays, which cannot penetrate more than about 1 cm. of tissue. Thus, localization of deeply situated tumors that concentrate P^{32} means inserting a probe counter into the region suspected to contain the lesion and necessarily coming ex-

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tremely close to the tumor in order to recognize the concentration of the isotope. This feature sharply restricts its use.

One might suspect that superficial tumors could be studied to advantage with P^{32}. Indeed, there are proponents of the use of P^{32} for localizing malignant melanomas in the skin (figure 12) or superficially placed malignant lesions of the breast. Others have found that localization by means of P^{32} is likely to be least helpful in cases in which diagnostic help is needed most. This is partly because the difference in radioactivity over the tumor and the adjacent normal tissue is often not large and partly because of the variation in concentration of P^{32} in normal skin, which is high over such regions as the forehead, lips and nipples.

Localization of P^{32} in a tumor has shown considerable promise in the diagnosis of optic tumors. A team of investigators at Western Reserve University has found that malignant tumors often can be distinguished from hemorrhage in patients with retinal detachment. The radiation is detected by a pencil-sized counter placed in direct contact with the eye (figure 13).

The greater penetrability of gamma rays through tissue over that of beta rays has led to many searches for gamma-emitting isotopes in elemental or compound form that will concentrate in tumors. When it was found that certain dyes were able to penetrate the blood-brain "barrier," such dyes were labeled with I^{131}. Increased radioactivity in the region of cerebral tumors located above the tentorium often was noted after the intravenous injection of labeled fluorescein; subtentorial tumors were less well recognized. Labeled dyes generally have been supplanted by serum albumin marked with I^{131}.

A new lead that offers promise in the study of brain tumors is the use of radioarsenic. Not only does arsenic seek out such tumors but the

FIGURE 12. Counting emanations from P^{32} in the skin of a patient with malignant melanomas. The Geiger-Müller tube is held in contact with the skin. The scaler records the radioactivity detected.

(From Owen, Charles A., Jr.: Diagnostic Radioisotopes, 1958. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.)

(Figures are numbered consecutively throughout the four parts of this article.)

FIGURE 13. A special type of Geiger-Müller tube designed to measure the rays from P^{32} localizing in optic tumors.

(From Owen, Charles A., Jr.: Diagnostic Radioisotopes, 1958. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.)

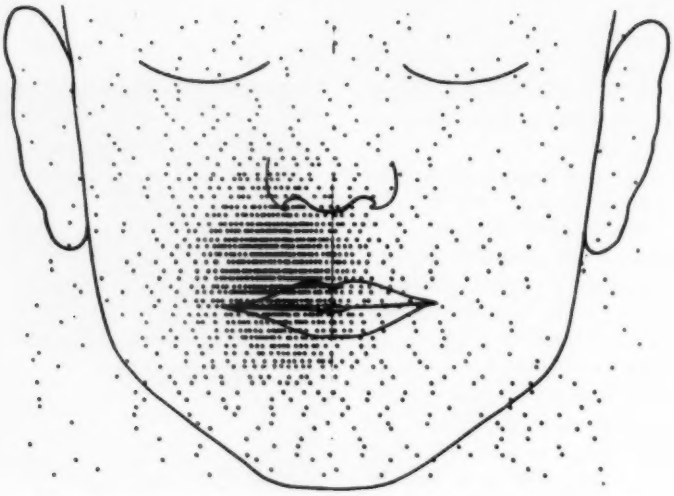


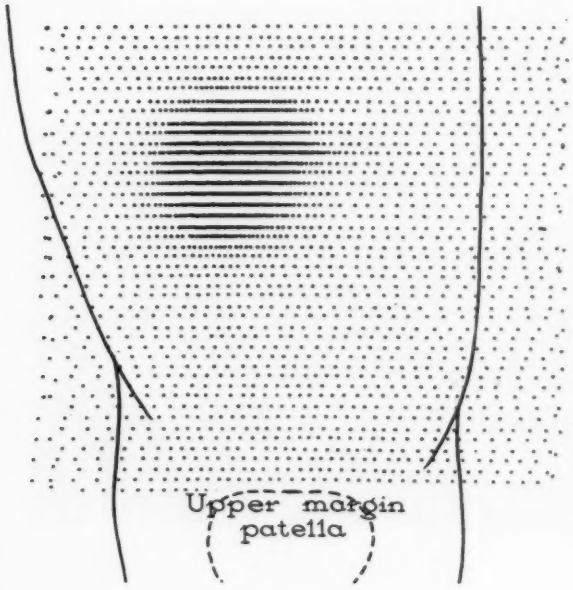
FIGURE 14. A scintiscan showing uptake of I^{131} in a tonsillar metastatic tumor in carcinoma of the thyroid.

(From Owen, Charles A., Jr.: Diagnostic Radioisotopes, 1958. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.)

radiation (positrons) is characterized by doubled rays projected in opposite directions. Paired radiation detectors "tuned" to the doubled rays only register an extremely low background, which has the effect of increasing the discrimination.

FIGURE 15. A scintiscan showing uptake of I^{131} in a metastatic tumor in the right femur in carcinoma of the thyroid.

(From Owen, Charles A., Jr.: Diagnostic Radioisotopes, 1958. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.)



Modification of scintillation counting in another direction already has proved its worth in evaluation of the thyroid. A scintiscanner consists of a scintillation detector moving back and forth along a fixed path until it has thoroughly scanned some predetermined area. Throughout its course, the scanner registers radioactivity by recording dots on a piece of paper; the more the radiation, the closer together are the dots. The completed patterns are called "gammagrams," "scintigrams" or "scintiscans." Examples of such patterns are shown in figures 14, 15 and 16; these were obtained and furnished by the Section of Therapeutic Radiology at the Mayo Clinic.

Not only may scintiscans localize unsuspected zones of thyroidal cells but they also may furnish an index to the functional state of nodules within a thyroid. For example, it is not unusual for a "hot" thyroidal nodule, one unusually avid for I^{131}, to be accompanied by almost complete depression of the function of the rest of the thyroid. Surgical removal of this type of nodule may not only relieve a patient of his hyperthyroidism but also permit the residual gland to regain normal func-

tion. On the other hand, when one can palpate a nodule in the thyroid that does not accumulate I^{131} ("cold" nodule), the possibility of a malignant lesion always comes to mind.

It has been suggested that the scanning technic may be useful in other regions of the body. After the intravenous injection of radioiodinated albumin or colloidal radiogold or certain labeled dyes, tumors or cysts within the liver stand out in sharp contrast to normal hepatic tissue ("hepatoscan"). A "cholecystiscan" is possible after the administration of radioactive rose bengal because this dye concentrates in a normally functioning gallbladder. In like vein, a protruding intervertebral disk may be located by means of labeled albumin injected into the subarachnoid space ("myeloscan").

Gastrointestinal Tract

A number of diagnostic tests are based on tracing a biologic pathway by labeling some substance that is normally involved. Two related tests designed to evaluate the enzymic activity of the pancreas are based on this principle. The substrates are tagged and given orally; triolein is used to measure pancreatic lipase, and albumin is employed for pancreatic protease. In either case, the radioactive label (I^{131}) is readily absorbed only if the protein or fat is digested. The absorption may be measured directly (I^{131} in the blood) or indirectly (excretion of absorbed I^{131} in the urine), as well as by difference (excretion of unabsorbed I^{131} in the feces).

A test of hepatic function comparable to the familiar sulfobromophthalein test reverts to the once widely used technic employing rose bengal. Since this dye is an iodinated compound, I^{131} may be incorporated into it. The labeled dye is given intravenously, and a continuous record is made of the radioactivity over the liver, high enough in the thorax to avoid the region of the gallbladder. Both the uptake and excretion of the dye are measurable and can be expressed as simple arithmetic rates. Since rose bengal is not so sensitive an indicator of hepatic dysfunction as is sulfobromophthalein, the test utilizing radioactive dye also may be of limited value, at least in the patient who does not have jaundice.

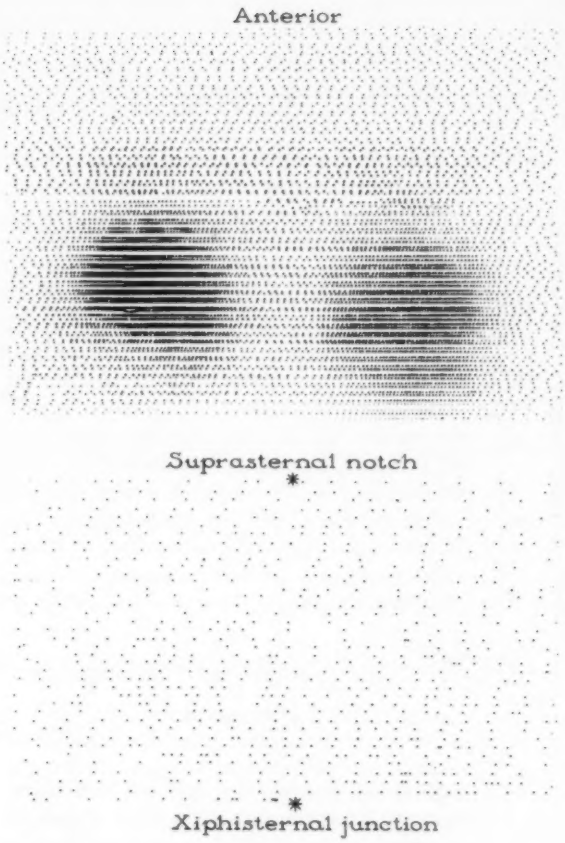


FIGURE 16. Scintiscans of the thorax of a patient with carcinoma of the thyroid and pulmonary metastasis. The lower scan suggests that the metastatic tumors had been eradicated by radioiodine therapy.

(From Owen, Charles A., Jr.: Diagnostic Radioisotopes, 1958. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.)

One of the more interesting tests is the evaluation of the error in metabolism of copper in Wilson's disease. The test is impractical, since Cu^{64} has a half-life of only about 13 hours and cases of hepatolenticular degeneration are too rare to warrant maintenance of a stockpile of the isotope. However, demonstration of the increased intestinal absorption and urinary excretion of salts of Cu^{64} is not difficult; more complex is the demonstration of abnormal binding of copper to serum proteins.

Mention already has been made of the feasibility of quantitating the amount of gas-

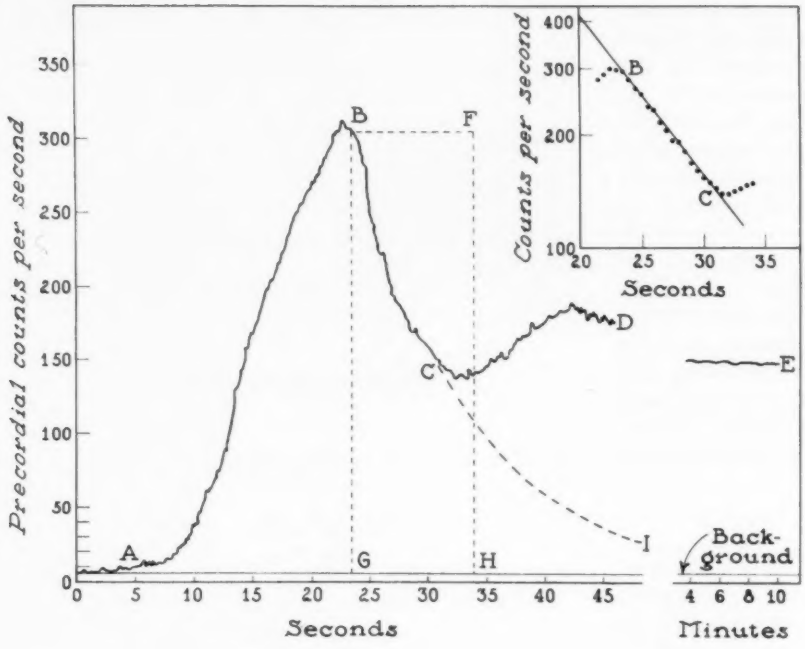


FIGURE 17. Record of radioactivity over the heart after the intravenous administration of human albumin labeled with I^{131}. The cardiac output can be calculated from these observations.

(From Owen, Charles A., Jr.: Diagnostic Radioisotopes, 1958. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.)

trointestinal bleeding by labeling the circulating erythrocytes with Cr^{51}. Only traces of radioactivity are evident in the feces of a Cr^{51}-labeled patient who is not bleeding. Thus, the finding of significant fecal Cr^{51} is as indicative of bleeding as are positive results of the guaiac test and is more specific. The fecal Cr^{51} may be expressed as milliliters of blood by comparing the radioactivity of feces with that of venous blood. The same principle holds true for Fe^{59}-labeled erythrocytes, but this probably will not be a widely used test since, as already noted, it takes the patient a week to label his own erythrocytes with radioiron.

Cardiovascular System

A number of procedures have been developed for measuring circulation times with radioisotopes; most of them apparently stress investigational goals rather than routine diagnosis. Certain tests eventually may become "routine," particularly as they offer a means of quantitating cardiovascular abnormalities.

Arm-to-leg circulation times are measured readily by placing a counter over a leg and injecting radiosodium or radioiodinated albumin into a vein in an arm. Not only is it possible to measure the time taken by the isotope to reach the leg but the "build-up" curve of radioactivity in the lower extremity may indicate the degree of vascular incompetence in such diseases as hypertension, scleroderma, Raynaud's disease or even frostbite. In patients who have hypertension, the response to sympathectomy can be anticipated by changes in the pattern of radioactivity effected by certain drugs that act on the autonomic nervous system.

One of the more important circulation times is that through the heart. By directing one or more radiation detectors toward the precordial region and injecting radioiodinated human albumin into an arm vein, it is possible to evaluate cardiopulmonary blood flow qualitatively and quantitatively as the injected isotope flows through the heart (figure 17). Whether the isotopic method can complement the conventional technics of cardiac catheterization requires further study.

An indirect test of vascularity may be of

some use to the surgeon in evaluating skin grafts. The slowed disappearance of an isotope such as Na^{24} or I^{131} injected into a graft signifies inadequate vascularity. In the case of a pedicle graft, the disappearance curve is little altered by clamping at the donor site if vascularity has become established.

Another indirect test of vascular supply may appeal to the orthopedic surgeon. When a fracture of the neck of the femur is to be treated by open reduction, it may be possible to prognosticate the success of the operation by means of P^{32}. When this isotope is administered intravenously, it will accumulate in the femoral head, as well as in the rest of the skeleton, only if a reasonably good vascular supply persists. By inserting a probe counter into a drill hole in the femoral head and comparing the radioactivity in this region with that in the trochanter, one can obtain a ratio. It is reported that such a head:trochanter ratio of as little as 1:10 invariably portends aseptic necrosis of the head because of the disruption of the circulation.

Renal Function

Although the process is technically complicated, a potentially useful "renogram" recently has been proposed. Two matched radiation detectors are directed at the kidneys (and away from the liver). Iodopyracet (DIODRAST®) labeled with I^{131} is injected into the blood stream, and the ability of the two kidneys to clear the Diodrast is compared. When a continuous record of the radioactivity is made, both the uptake and excretion of the Diodrast can be related. It has been suggested that this technic might be a time-saving approach to the problem of evaluation of hypertension in younger patients; only if one kidney shows an abnormal clearance pattern is a complete urologic examination required. One also could imagine the application of this test to patients with renal "shutdown."

Electrolytes and Water

Of great potential usefulness in diseases of the heart, kidneys, adrenals and gonads is the measurement of body water. The clinical diagnosis of imbalance in the water compartments of the body, such as edema, is generally crude. The extracellular space can be quantitated with radiosodium, the intracellular space with radiopotassium or radiorubidium, and the total body water with tritiated water ($H^3{}_2O$). The plasmatic portion of the extracellular space is simply measured as the "plasma volume" by use of radioiodinated albumin. The drawbacks to widespread use of measurement of these spaces are the short half-lives of Na^{24} and K^{42} (each about half a day) and the difficulty of measuring tritium except by means of expensive, refrigerated, liquid-scintillating counters.

Comment and Conclusions

With an increasing number of young investigators receiving accreditation from the Atomic Energy Commission for use of radioactive isotopes, rapid advances in the research aspects of isotopes may be expected. A certain fraction of these newer procedures inevitably will find its way into the diagnostic radioisotope laboratory.

A representative group of presently accepted methods has been reviewed in this series of papers. It is obvious that these methods involve gamma-emitting radioisotopes almost exclusively. Yet the elements most closely associated with the building stones of living material, such as carbon, hydrogen, oxygen, nitrogen, phosphorus and sulfur, do not have convenient isotopes that emit gamma rays. With the development of equipment that will measure the beta ray isotopes of certain of these elements more simply than is presently possible, major advances in diagnostic procedures may be expected.

Calories

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At a time when so much of the physician's and dietitian's attention is devoted to weight reduction, it probably would be helpful to recall that the primary nutritional requirement is the need for calories. Caloric undernutrition, if sufficiently prolonged, is such an overriding factor that no diet can be considered adequate unless the energy balance is considered—a fact which should be drilled into the consciousness of many patients, particularly teen-age girls desiring to be excessively slim and nursing mothers determined to recover their figure as soon as possible.

I can think of few words as commonly used with as little understanding of meaning as the word "Calorie."† Readers will remember that the Calorie, or kilocalorie, is the amount of heat energy which is required to raise the temperature of 1 kg. of water 1° C., from 14.5 to 15.5° C., and that the caloric equivalent of mechanical energy may be calculated by multiplying the units of mechanical energy (joules) by the factor 4.18. It is probably important to pause at this point, however, and reflect on the fact that many patients have never thought of the first law of thermodynamics or about the equivalence of chemical potential energy in foods, mechanical energy in physical exercise, and chemical energy used in synthesis of tissues, milk or body fat. Thus, it is essential that this concept be made clear to them before any further dietary instruction can be given profitably. The idea that five slices of white bread, an hour of walking at moderate speed, and an ounce of body fat are roughly equivalent from an energy standpoint is not as readily understood by patients as busy practitioners would like to believe.

Food Composition

The main sources of calories for man are carbohydrate, fat and protein. Again, from the viewpoint of energy, the three foodstuffs are interchangeable in accordance with their caloric equivalent. This was first shown by Rubner and further elaborated in this country by

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†Properly speaking, Calorie, the unit used in nutrition, should always be spelled with a capital "C" when a measure of intake or output is given. The word "calorie" with a small "c" refers to the gram-calorie, a thousandth of the Calorie. The word "calorie" can be used when speaking of calories in general. In fact, the distinction is often not made, and calorie with a small "c" is often used improperly in lieu of Calorie.

Atwater and his collaborators at the beginning of this century. These workers determined not only the composition of all common American foodstuffs but also their digestibility; thus, they could determine with great precision their energy content. They found that the proteins, fats and carbohydrates contained in the various foods were not strictly equivalent gram for gram from the viewpoint of energy; for example, a gram of starch contains a little more energy than a gram of glucose, and a gram of steak protein has a little more energy than a gram of protein from bread. However, such differences are small, so that when we consider the usual mixed diets, such as those consumed in this country, an excellent approximation of the total energy content can be obtained by using the caloric equivalents four, nine and four for carbohydrate, fat and protein, respectively. Further, these "net caloric factors" consider digestibility and can be applied as such to the composition of the whole diet.

Food composition tables are still prepared along the same principles. In the United States, the tables usually seen by practicing physicians are reproductions, summaries and adaptations of the food composition tables prepared by the United States Department of Agriculture. The famous blue booklet[1] issued by this department gives the caloric value of 751 foods in terms of pounds "as purchased," "common household units" (slices, cupfuls, portions, etc.), and in 100 gm. edible portions. For anyone interested in diet analysis, this handbook is a constant reference.

It must be realized that the availability of data concerning a given foodstuff is not sufficient to assess the caloric content of a dish based on this foodstuff. Actual samples may differ widely in composition from the average value published in the food composition table. For example, the composition of a certain variety of pears consumed in August is unlikely to coincide with the median values for 50 varieties of pears consumed during a large part of the year all over the United States. The weight of the latter is calculated on the basis of survey data on varieties consumed in larger quantities over longer periods. The variability in caloric content is likely to be even much greater in cuts of meat than in fruits. Variations in fat content which appear small in terms of dry weight from animal to animal and from cut to cut will be translated into large differences in caloric equivalents. In addition, individual cooking practices vary: Some cooks will add butter when cooking steak; others will not. The drippings may or may not be eliminated from the dish as served.

Finally, individual attitudes toward table fats are difficult to ascertain. Some patients will cut the fat from ham; others will eat the whole slice. Some patients eschew gravy; others eat liberal quantities, using bread to avoid wasting any. Such differences in practice may entail 100 per cent differences in the actual caloric content of two consumed portions of what appeared to be, a priori, the same dish.

Children present a particularly difficult problem because of the greater variability of their attitudes and appetites. Unless these causes of variations are investigated and the results quantified, the appraisal of a diet is worthless from the viewpoint of caloric intake, even though a more cursory evaluation can still be valuable from the viewpoint of less variable nutrients.

Components of Energy Expenditure

The appraisal of caloric balance is rendered even more difficult by the fact that energy output depends on a number of factors other than intake, some of which may vary from day to day. Classically, the components of energy expenditure are (1) basal metabolism, (2) specific dynamic action, (3) extra heat production for maintenance of body temperature in a cold environment, (4) physical activity, and (5) growth, tissue repairs, pregnancy and lactation.

Basal metabolism—Basal metabolism represents the energy expenditure of the fasting resting subject as thermal neutrality—about 25° C. The familiar clinical determination is conducted on the person who is awake and lying at rest at a comfortable temperature at least 14 hours after ingesting food. Other things being equal, larger persons show a

greater basal metabolic rate (B.M.R.) than smaller persons, the difference being roughly proportional to the difference in body surface.

A number of theoretical and empirical formulas have been proposed to express this "surface law." The empirical equation of DuBois and DuBois is most often used in the United States. The index obtained by dividing the basal metabolism by the body surface is the well-known basal metabolic rate, a parameter found to be characteristic for healthy individuals of the same age and sex. Basal metabolic rate values for women are about 10 per cent smaller than those for men of the same size, a fact which has been ascribed to the finding that kilogram for kilogram the active body mass of women is smaller than that of men; i.e., women's bodies are normally higher in fat and lower in protein than are men's bodies. Basal metabolic rates decrease slowly with age. For example, the rate for a 35 year old man is usually about 40 calories per square meter per hour. (The body surface of the 155 lb. man is slightly under 2 sq. m.) The same person at age 65 will usually show a B.M.R. of about 35 calories per square meter per hour. Again this decline is ascribed to the fact that even if there is no weight change in the intervening 30 years, a shift of body composition occurs, so that the body of the 65 year old man contains less protein and more fat than it did at age 35.

The basal metabolic rate is often expressed in terms of percentage above or below the normal B.M.R. standards. A rate of +10 corresponds to a basal heat production of 10 per cent above the standard; a rate of −15 corresponds to a basal heat production of 15 per cent below the standard. In using these standards, it is well to remember the following facts:

1. The current standards are based mostly on averages of first tests and give values 5 to 10 per cent too high when compared with values obtained with trained subjects. This has been confirmed in particular by E. F. DuBois.

2. The empirical formula used as a basis for the standards was based on data obtained for persons of various weights (including overweight persons) considered clinically to be free from disease, particularly thyroid diseases, and devised in such a way that the formula would give a good representation of their basal metabolism. To reverse the situation, as has occasionally been done, and say, "Most obese persons have a B.M.R. which fits the basal metabolism formula, and, therefore, their metabolism is normal," is not a legitimate proposition for two reasons. The formula was established so that the persons examined who were free from thyroid disease would fit it, and the word "metabolism" is being used with two very different meanings. The basal metabolism of most diabetic persons is normal, yet their metabolism is not.

3. Small variations—particularly, downward variations—from the standards have no diagnostic significance per se and should not be used to justify thyroid therapy without additional supporting evidence (e.g., protein-bound iodine, thyroid iodine uptake, clinical signs and symptoms). This is especially important in considering children and adolescents, for whom B.M.R. standards and interpretations are particularly uncertain, and obese individuals, in whom not only weight and surface (taken into account in the standards) but also body composition (proportion of active body mass) may be very abnormal.

In a recent survey conducted in the Adolescent Clinic of the Children's Hospital in Boston, it was found that many obese adolescents who had been "put on thyroid" by their physician did not exhibit any hypothyroidism when subjected to thorough clinical and metabolic appraisal. Thyroid or thyroxin therapy without convincing prior diagnosis of hypothyroidism is a highly questionable practice.

It has often been stated that, in addition to its influence on the component of energy expenditure concerned with maintaining body temperature in the cold, basal metabolism is depressed by prolonged exposure to a warm climate and elevated by exposure to a cold climate. The evidence is poor and contradictory. It appears that if the B.M.R. is measured, as it should be, in a thermoneutral environment climate has no significant effect on basal metabolism. Claims of racial differences in the B.M.R. have never been substantiated.

Specific dynamic action—The simple ex-

perimental concept of specific dynamic action (S.D.A.) is usually taught in such a way as to give the medical student a confused impression which opens his mind, when he becomes a practitioner, either to beliefs of exaggerated variability of this parameter (particularly in relation to high protein diets) or, possibly by reaction, to the curious conviction that the existence of the S.D.A. has been "disproved." Actually, all that is involved is that the recent ingestion of food by a resting individual in a comfortable environment brings about an increase in heat production and heat loss, which is called the specific dynamic action of the foodstuffs ingested.

It is true that when single nutrients are ingested under laboratory conditions there are differences between the S.D.A. of proteins (ingesting 100 calories of protein raises the heat production by 30 calories, leaving 70 net calories available—a 30 per cent S.D.A.), that of carbohydrates (8 to 10 per cent), and that of fat (4 to 6 per cent). However, the S.D.A. of mixed meals—the only ones of practical dietary significance—varies between relatively narrow limits (about 10 to 15 per cent). In other words, the S.D.A. of a meal is not the sum of the specific dynamic action of the carbohydrates, fats and proteins contained in the meal. High protein meals may be preferable to low protein meals in certain circumstances, particularly in reducing diets. But it is *not* because the S.D.A. of the two types of diet represents an appreciable caloric fraction.

Heat production and heat loss—One of the most fundamental facts about man is that he is homothermal, i.e., an organism which regulates its body temperature within a very narrow range. Deviations from the normal have a diagnostic significance; if they are excessive in either direction, they may be fatal. The nature and function of the thermostat through which a constant temperature of $37 \pm 0.5°$ C. is achieved in man is still largely unknown. My investigation in collaboration with T. R. A. Davis showed that two types of control of heat production seemed to be involved: a non-muscular (chemical) thermogenesis, apparently regulated by the variations of internal temperature, and a muscular (physical) thermogenesis, expressly from shivering and apparently regulated by differences between internal and skin temperatures.

The mechanism of heat loss, the other factor in the balance, is better known. Heat loss from a resting man occurs through radiation and convection, through the latent heat of evaporation of water through the skin and lungs (the so-called insensible perspiration already demonstrated by Sanctorius at the end of the sixteenth century), and through the warming of inspired air and of ingested food and water. This heat loss is a function of many factors other than the environmental temperature. Clothing, wind, humidity, time spent indoors, etc. combine to define the individual "micro-environment" and the "effective temperature" at which a given subject lives.

In trying to evaluate the quantitative effect of temperature on human energy needs, the first and second committees on Calorie requirements called by the Food and Agriculture Organization of the United Nations and the World Health Organization had available the results of a study of United States and Canadian soldiers stationed in various parts of the world in which geographical situations ranged from arctic to dry and tropical environments. The study showed a linear relationship between decreasing environmental temperature and increasing caloric intake. This principle of linearity was retained by the first Calorie committee for calculations on civilian populations. Deviations from this relationship were observed in practice. The second Calorie committee estimated that for the general population the caloric requirement increases by 3 per cent for each 10° C. below an average mean annual temperature of 10° C. (typified by Minneapolis), and it decreases by 5 per cent for each 10° C. above this average. The difference results from the fact that man protects himself better against cold than against heat. The recommendations of these committees were essentially adopted by the Food and Nutrition Board of the United States Research Council.

When trying to estimate the caloric requirements of an individual patient, the physician can use such figures only as a very general

guide and should estimate the amount of actual exposure to outside temperatures. Thus, even in a cold environment, for example, Chicago in the winter, the amount of actual exposure to cold for an individual commuting in a heated car from home to office may be negligible.

Physical activity—Physical activity is the most variable component of the total energy expenditure. It can be subdivided into two types: that related to body size (walking, moving the arms and hands, etc.) and that unrelated to body size (lifting and pushing objects). The first component is roughly proportional to body weight; the second is influenced only very little by body weight.

An enormous amount of experimental work, started in the nineteenth century and pursued throughout this century, has made available the energy cost of all the usual occupations, games, household chores, etc. Knowing the schedule of a given individual, it is now possible to estimate his energy expenditure. It is true that skill and training will modify the expenditure required by a given task or exercise; it is also true that the "microschedule," the number and duration of pauses during a given task or exercise, also should be considered in such estimates. Still the available data make it possible for an experienced physician or nutritionist to arrive at a moderately good idea of how many calories a given individual expends every day, an operation which is essential in prescribing a reducing diet in which, after all, the magnitude of the caloric *deficit* is only estimated. As is well known, the considerable differences in the cost of activities, ranging from 10 calories (writing) to 700 calories (sawing) or more per hour, lead to differences in allowances which range from 2400 calories per day for a sedentary man to 4500 calories for a very active man, with a rare maximum of 6000 or more for the most strenuous athletic or other extremely arduous occupations. Tables giving the expenditure corresponding to various occupations have been published by Passmore and Durnin.[2]

It is essential that the physician or dietitian who is trying to determine the energy expenditure of a patient pay particular attention to

TABLE 1

CALORIES USED IN DAILY ENERGY EXPENDITURE

Case 1—A 25 year old, 154 lb. house painter living in a suburb of Minneapolis, which has a mean annual temperature of 10° C.	
Working activity (10 hours)	
8 hours standing and painting (3 calories per minute)	1,450
2 hours gardening or sports (5 calories per minute)	600
Nonoccupational activity (6 hours)	
1 hour washing, dressing, etc. (2.5 calories per minute)	150
4 hours driving, sitting, etc. (1.7 calories per minute)	400
1 hour domestic work (3.5 calories per minute)	200
Rest in bed at B.M.R. (8 hours)	500
TOTAL	3300
Case 2—A 50 year old, 170 lb. office worker living in Minneapolis	
Working activity (8 hours)	
Office work, sitting (1.6 calories per minute)	760
Nonoccupational activity (8 hours)	
1 hour washing, dressing, etc. (3 calories per minute)	180
6 hours driving, sitting (1.8 calories per minute)	640
1 hour domestic work, standing (2.5 calories per minute)	150
Rest in bed at B.M.R. (8 hours)	500
TOTAL	2200
Case 3—A 21 year old, 121 lb. housewife, lactating, living in California, which has a mean annual temperature of 20° C.	
Working activity (10 hours)	
Domestic work, care of baby, etc. (2 calories per minute)	1200
Nonoccupational activity (6 hours)	
1 hour washing, dressing, etc. (2 calories per minute)	120
1 hour walking at 3 mph and shopping (3.2 calories per minute)	200
2 hours playing golf or gardening (3.0 calories per minute)	360
2 hours sitting (1.2 calories per minute)	140
Rest in bed at B.M.R. (8 hours)	400
Lactation allowance (600 to 700 cc. milk)	800
TOTAL	3200
Case 4—A 35 year old, 132 lb. housewife living in Minneapolis	
Working activity (8 hours)	
Domestic work (1.9 calories per minute)	910
Nonoccupational activity (8 hours)	
1 hour washing, dressing, etc. (2 calories per minute)	120
1 hour shopping and driving (1.8 calories per minute)	100
6 hours sitting (1.3 calories per minute)	470
Rest in bed at B.M.R. (8 hours)	400
TOTAL	2000

TABLE 2

DAILY DIETARY ALLOWANCES FOR CALORIES*

SUBJECTS	AGE (years)	WEIGHT (kg.)	WEIGHT (lb.)	HEIGHT (cm.)	HEIGHT (in.)	CALORIES
Men	25	70	154	175	69	3200
	45	70	154	175	69	3000
	65	70	154	175	69	2550
Women†	25	58	128	163	64	2330
	45	58	128	163	64	2200
	65	58	128	163	64	1800
Infants	0 to 1/12					
	2/12 to 6/12	6	13	60	24	kg. x 120
	7/12 to 12/12	9	20	70	28	kg. x 100
Children	1 to 3	12	27	87	34	1300
	4 to 6	18	40	109	43	1700
	7 to 9	27	60	129	51	2100
	10 to 12	36	79	144	57	2500
Boys	13 to 15	49	108	163	64	3100
	16 to 19	63	139	175	69	3600
Girls	13 to 15	49	108	160	63	2600
	16 to 19	54	120	162	64	2400

*Allowances for normally active persons in a temperate climate, according to 1958 revised recommendations of the Food and Nutrition Board, National Research Council.

†A woman in the second half of pregnancy should have +300 calories daily. A woman with a daily lactation of 850 ml. should have +1000 calories.

time spent on each major occupation as well as to cost. If the time spent at rest in bed, sitting, standing, walking, occupation requiring physical effort, and sports is accurately recorded, other incidental energy expenditures are secondary. The mere designation "farmer" or "miner" gives very little information on the energy expenditure of the patient. A farmer may have a wide range of physical activities, depending on his job on the farm, the type of farming, and the extent of mechanization. Similarly, a miner is anyone who works in a mine. He may use a pick and shovel, carry and handle a pneumatic drill, or sit at a desk keeping track of coal cars coming out of a gallery.

Christensen has classified physical work in five categories: very light work (office work), less than 2.5 calories per minute; light work (leisurely walking, painting), 2.5 to 4.9 calories per minute; moderate work (brisk walking, light plumbing work, laying bricks), 5.0 to 7.4 calories per minute; heavy work (blacksmithing, bicycling, skating), 7.5 to 9.9 calories per minute; and very heavy work (swimming, climbing, shoveling), more than 10 calories per minute. These classifications can be used to establish an approximate picture of a man's daily expenditure (table 1).

Growth—Growth in its broadest sense (body growth, repairs, pregnancy, lactation) is accompanied by an increase in energy requirements. The caloric requirements of children are given in table 2. It must be noted that these are extremely approximate in that the variability of activity in children is such that the standard deviation is probably about one-fourth the expenditure. In other words, many children will require 25 per cent more calories than the average, and a substantial proportion of children will require more than 50 per cent more than the average because of their activity.

Pregnancy has been calculated to correspond to an increased requirement of about 80,000 calories for the over-all nine month period. The extra calorie needs imposed by pregnancy can, however, be covered in two ways: either by increased food intake or, in part at least, by reduced physical activity. The balance between the two is determined by the personal habits, conditions of employment, presence of older children to be cared for, etc. A few women will thus require the full amount

of extra calories as food. This would correspond to an average of 300 calories extra per day or, more generally, no increase during the first trimester and an increase of 400 to 500 calories during the next two trimesters. However, most women will achieve the desired weight increase of approximately 20 lb. for the entire pregnancy with a much smaller increase in food intake. In fact, in our society many women will achieve this increase solely on the basis of decreased physical activity. This has important consequences for the practicing obstetrician: If an extracaloric intake corresponds to excessive weight gain during pregnancy for such women, the obvious way to improve their diet is not simply by prescribing additional milk, eggs, etc., but by eliminating some of the "empty" calories and replacing them with foodstuffs of higher nutritional values.

The problem of lactation is one which is particularly important and often neglected. Obstetricians have a strong tendency to stress the importance of a good diet during pregnancy and to neglect to check the diet during lactation. Yet the daily accretion of tissue during pregnancy represents a much smaller nutritional stress than the secretion of large quantities of milk (850 ml. milk corresponds to about 1000 calories). The lactation period also usually represents a time of return to normal activity; in fact, very often it is a time of increased physical activity. In addition to previous commitments, the mother must take care of a small baby, so that caloric compensations by inactivity no longer occur. The pregnant woman could not ignore her physiologic state, especially during the last trimester of pregnancy, and "took care of herself" for fear of harming her unborn baby; however, the lactating mother has a tendency not to worry any more about her nutrition, even though she has to provide more protein, more calcium, etc. Too often she wants to get back "as fast as possible" to her prepregnancy figure. The physician must remember that the caloric requirement during lactation is dominated by the amount of milk output. For satisfactory lactation the increment over the normal intake should be not less than 800 calories per day.

The next discussion in this series will deal with a more specialized aspect of the subject of calories: the relation of exercise to weight control.

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MEETINGS *and Postgraduate Courses*

American College of Allergists, San Francisco: Graduate instructional course and annual congress, March 15-20, at the Mark Hopkins Hotel. For further information, write to: Dr. John D. Gillaspie, 2049 Broadway, Boulder, Colorado.

American College of Surgeons, St. Louis: Sectional meeting, March 9-12, at Kiel Auditorium. For further information, write to: Dr. H. Prather Saunders, Associate Director, American College of Surgeons, 40 East Erie Street, Chicago 11.

Association of the National European and Mediterranean Societies of Gastroenterology, Leiden, Netherlands: Sixth meeting, April 20-24, 1960. For further information, write to: Congress Office of the Sixth Meeting of the Association of the National European and Mediterranean Societies of Gastroenterology, University Hospital, Leiden, Netherlands.

Ninth International Congress of Radiology, Munich, Germany: July 23-30. For further information, write to: Congress Secretariat, Reitmorstrasse 29, Munich 22.

Second World Conference on Medical Education, Chicago: August 31-September 4 at the Palmer House. Sponsored by the World Medical Association. For further information, write to Dr. Louis H. Bauer, Secretary General, The World Medical Association, 10 Columbus Circle, New York 19.

Comparison of the Diuretic Effects of Oral Administration of Chlorothiazide and Parenteral Administration of Mercaptomerin

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THERE is a need for a potent, orally effective, nonmercurial diuretic which is well tolerated. In order to give additional clinical information supporting previous bioassay studies,[1] a study was made to determine the comparative diuretic properties of orally administered chlorothiazide (DIURIL®) and parenterally administered mercaptomerin (THIOMERIN®). This report presents data concerning the effect of these two drugs in man on serum electrolyte levels and on the excretion of sodium and water under clinical conditions of therapeutic need.

Material and Method of Study

The two diuretics were administered to 20 edematous male patients who had cardiac disease or cirrhosis. The patients were at rest in bed, and they were fed a diet which contained 800 mg. of sodium. The ingestion of water was controlled at 3000 ml. each 24 hours. If the patients previously had been taking digitalis or antihypertensive drugs, the dose of these drugs remained constant throughout the period of the study.

Each patient was observed for 12 days, which were divided into four periods of three days each, namely, a first control period, a period of administration of the first drug, a second control period, and a period of administration of the second drug. Thus, the first control period was followed by a period of three days during which one group of 10 patients were given 2000 mg. of chlorothiazide orally each day and another group of 10 patients received 2 cc. of mercaptomerin parenterally. The second control period of three days followed, and the order of administration of the diuretics was reversed in both groups.

The values for the sodium, potassium and chloride in the serum and the carbon dioxide-combining power were determined once in each period. The volume of urine excreted in each 24 hours was recorded, and the daily excretion of sodium was determined. Teleroentgenograms and electrocardiograms were made at the beginning and at the completion of the

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study. The weight of the patients was recorded each day.

Results

Changes in volume of urine, excretion of sodium, and body weight—In the group of cases in which the administration of chlorothiazide was followed by the administration of mercaptomerin, the average weight of the patients in the first control period was 185 lb. On the first, second and third days following the administration of chlorothiazide, the weights were 180, 182 and 177 lb., respectively. During the three following days, no diuretic was given and the average weight increased to 180 lb. Mercaptomerin therapy then resulted in a weight reduction to 177, 180 and, finally, to 176 lb. during the next three days (table 1).

In the first control period, the urinary excretion of sodium averaged 35 mEq. in 24 hours (figure 1). On subsequent days of chlorothiazide administration, it increased to 125 and 134 mEq., while on the third day it dropped slightly to 115 mEq. During the following three days, no diuretic was given, and the urinary excretion of sodium averaged 15 mEq. in 24 hours. Mercaptomerin therapy then resulted in an increase in the urinary excretion of sodium to 67, 69 and 50 mEq. per 24 hours in the three days during which the drug was administered.

TABLE 1

COMPARISON OF URINARY EFFECTS AND CHANGES IN BODY WEIGHT DUE TO ORAL ADMINISTRATION OF CHLOROTHIAZIDE AND INTRAMUSCULAR ADMINISTRATION OF MERCAPTOMERIN*

	C	*D-1*	*D-2*	*D-3*	*C-2*	*D-2₁*	*D-2₂*	*D-2₃*
CHLOROTHIAZIDE FOLLOWED BY MERCAPTOMERIN								
Excretion of sodium *(mEq. per 24 hr.)*	35	125	134	115	15	67	69	50
Amount of urine *(liters per 24 hr.)*	2.4	3.2	2.8	3.0	2.6	3.2	3.1	2.9
Body weight *(pounds)*	185	180	182	177	180	177	180	176
MERCAPTOMERIN FOLLOWED BY CHLOROTHIAZIDE								
Excretion of sodium *(mEq. per 24 hr.)*	35	95	105	85	20	90	95	75
Amount of urine *(liters per 24 hr.)*	2.2	2.3	2.3	2.2	1.9	3.0	2.6	2.5
Body weight *(pounds)*	169	169	167	166	163	160	160	163

*Average for 10 patients.

Key to table: *C*, first control period; *D-1*, *D-2* and *D-3*, consecutive days of administration of first drug; *C-2*, second control period; *D-2₁*, *D-2₂* and *D-2₃*, consecutive days of administration of second drug.

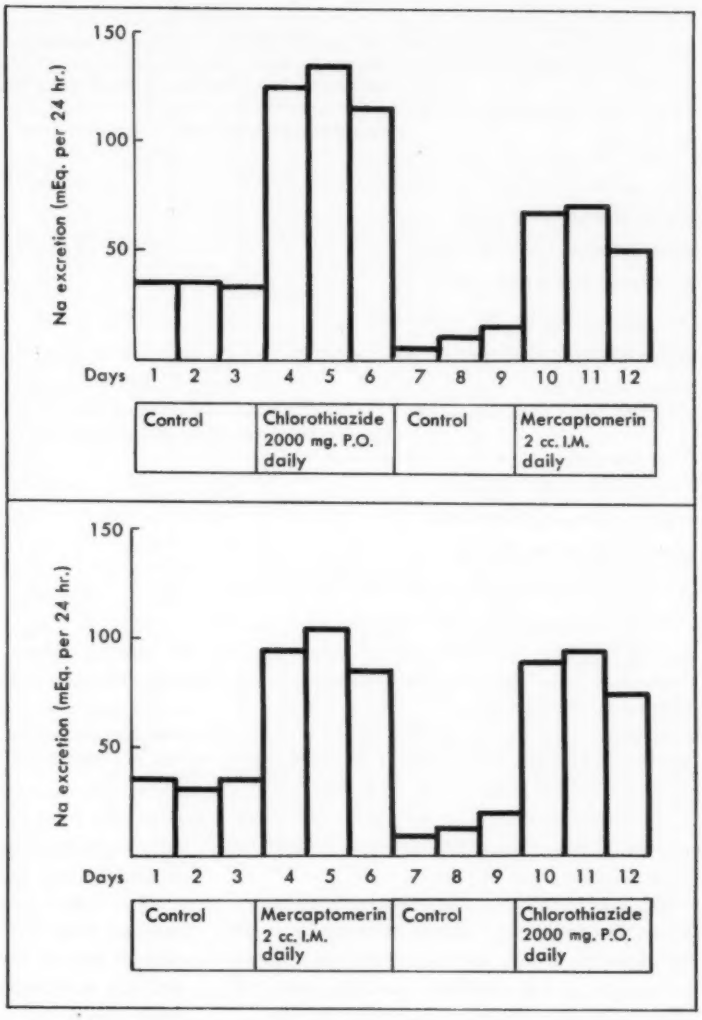

FIGURE 1. Comparative effects on sodium excretion of orally administered chlorothiazide and intramuscularly administered mercaptomerin.

In the group of cases in which the administration of mercaptomerin was followed by the administration of chlorothiazide, the weight of the patients in the first control period averaged 169 lb. The weight remained the same on the first day of administration of mercaptomerin, but it decreased to 167 on the second day and to 166 on the third day. In the second control period, the average weight was 163 lb. Thus, there was an additional loss of weight in the three days following the administration of mercaptomerin. In the three days on which chlorothiazide was administered, the weight of the patients decreased to 160, 160 and 163 lb., respectively.

In the first control period in this group of cases, the average excretion of sodium in the urine was 35 mEq. in 24 hours. It increased to 95, 105 and 85 mEq., respectively, during the next three days in which mercaptomerin was administered. It decreased to 20 mEq. on the third day of the second control period. During the next three days in which chlorothiazide was administered, the urinary excre-

TABLE 2

COMPARISON OF EFFECTS OF ORAL ADMINISTRATION OF CHLOROTHIAZIDE AND INTRAMUSCULAR ADMINISTRATION OF MERCAPTOMERIN ON SERUM ELECTROLYTES, BLOOD UREA NITROGEN, CARBON DIOXIDE-COMBINING POWER AND HEMATOCRIT READING*

	C	*D*	*PD*	*C-2*	*D-2*	*PD-2*
CHLOROTHIAZIDE FOLLOWED BY MERCAPTOMERIN						
Serum sodium *(mEq. per liter)*	138	138	137	137	137	138
Serum potassium *(mEq. per liter)*	5.3	5.0	4.7	4.7	4.9	5.4
Serum chloride *(mEq. per liter)*	95	93	91	91	93	96
Urea nitrogen *(mg. per 100 cc. of blood)*	19	19	24	24	20	20
Carbon dioxide-combining power *(mEq. per liter)*	29	29	30	30	30	30
Hematocrit reading	45	45	44	44	43	48
MERCAPTOMERIN FOLLOWED BY CHLOROTHIAZIDE						
Serum sodium *(mEq. per liter)*	139	141	137	137	140	141
Serum potassium *(mEq. per liter)*	4.5	4.7	4.5	4.5	4.5	4.4
Serum chloride *(mEq. per liter)*	94	92	92	92	93	91
Urea nitrogen *(mg. per 100 cc. of blood)*	20	17	16	16	19	13
Carbon dioxide-combining power *(mEq. per liter)*	29	29	29	29	29	29
Hematocrit reading	45	48	50	50	48	46

*Average for 10 patients.

Key to table: *C*, first control period; *D*, second day of administration of first drug; *PD*, second day after administration of first drug was discontinued; *C-2*, second control period; *D-2*, second day of administration of second drug; *PD-2*, second day after administration of second drug was discontinued.

tion of sodium increased to 90, 95 and 75 mEq., respectively (figure 1).

Changes in serum electrolytes, urea nitrogen of the blood, and hematocrit reading—In the cases in which administration of chlorothiazide was followed by administration of mercaptomerin, the average value for the serum sodium in the first control period was 138 mEq. per liter, and this did not change significantly (table 2; figure 2). The value for the serum chloride, which was 95 mEq. per liter in the first control period, decreased to 93 mEq. per liter on the second day on which chlorothiazide was administered, and it decreased to 91 mEq. per liter on the second day after the administration of this drug was stopped. On the second day on which mercaptomerin was administered, the value for the serum chloride was 93 mEq. per liter, and it continued to increase until it reached 96 mEq. per liter on the second day after the administration of mercaptomerin was stopped.

The value for the serum potassium decreased from 5.3 mEq. per liter in the first control period to 5 mEq. per liter on the second day on which chlorothiazide was administered and to 4.7 mEq. per liter on the second day after the administration of this drug was stopped. However, it increased to 4.9 mEq. per liter on the second day on which mercaptomerin was administered and to 5.4 mEq. per liter on the second day after the administration of this drug was stopped (table 2). The carbon dioxide-combining power increased slightly after the administration of chlorothiazide but it remained constant after the administration of mercaptomerin. The hematocrit reading remained essentially unchanged after the administration of chlorothiazide, but it increased from 43 on the second day on which

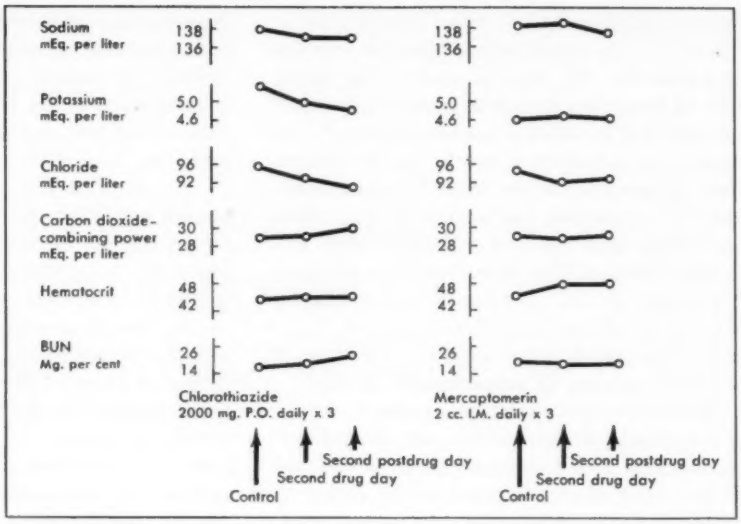

FIGURE 2. Comparative effects of chlorothiazide and mercaptomerin on blood electrolytes, hematocrit and blood urea nitrogen.

mercaptomerin was administered to 48 on the second day after the administration of the drug was stopped.

In the cases in which the administration of mercaptomerin was followed by the administration of chlorothiazide, the average value for the serum sodium was 139 mEq. per liter in the first control period, and it did not change significantly. The value for the serum potassium showed very little change. The value for the serum chloride decreased from 94 mEq. per liter in the first control period to 92 mEq. on the second day on which mercaptomerin was administered, and it remained constant in the second control period. On the second day on which chlorothiazide was administered, the value increased to 93 mEq. per liter, but it decreased to 91 mEq. per liter on the second day after the administration of this drug was stopped. The carbon dioxide-combining power remained unchanged. The hematocrit reading increased slightly, but there was no significant change in the blood urea nitrogen.

Comment

Many types of diuretics are available.[2,3] Those used most commonly are the mercurial diuretics (MERCUHYDRIN®, NEOHYDRIN®, THIOMERIN®, etc.), the carbonic anhydrase inhibitors (DIAMOX®), and the aminouracils (MICTINE® and ROLICTON®). A potency of 1 has been assigned to a "standard" diuretic agent, meralluride (Mercuhydrin). The mercurial diuretic chlormerodrin (Neohydrin) is well tolerated when administered orally, but it is only half as potent as meralluride when the latter drug is administered parenterally. It has been shown that when acetazolamide (Diamox) is administered orally it is an active carbonic anhydrase inhibitor and that it has a potency of 0.25. Since it causes a significant metabolic acidosis and hypokalemia, it must be used cautiously in the treatment of cirrhosis, edema due to steroid therapy, and nutritional edema.

Aminometradine (Mictine) has a potency of 0.7, and is effective when administered orally. However, tolerance to the drug develops rapidly, and it is necessary to administer the drug on an interrupted schedule. The same is true of the carbonic anhydrase inhibitors. Chlorazanil (DAQUIN®), which has a potency of slightly less than 0.5, is a mild natruretic agent of a different chemical class (triazine). Although it does not cause any significant disturbance in the serum electrolytes, it has one serious drawback; namely, it occasionally causes an increase in the blood urea nitrogen.

Chlorothiazide (6-chloro-7-sulfamyl-1,2,4-

benzothiadiazine-1, 1-dioxide) is a potent inhibitor of the renal reabsorption of sodium and chloride, and since it produces an excretion of these ions in approximately equivalent quantities it is called a saluretic agent. Potassium is excreted to a much smaller degree than sodium or chloride, while bicarbonate excretion is minimal. The action occurs within two hours after the oral administration, and it lasts 12 hours. This agent has been assigned a potency of 0.8.[4] Continued use of chlorothiazide produces a tendency toward hypochloremic, hypokalemic alkalosis; however, it responds quickly to supplemental therapy.

Mercaptomerin, which has a potency of 0.6,[1] is a mercurial diuretic which acts (by inhibiting succinic dehydrogenase) in the distal part of the renal tubule. It prevents the reabsorption of sodium and chloride, and causes excretion of sodium, chloride and water. There is no significant potassium loss, and bicarbonate excretion is temporarily suppressed. The onset and duration of action are approximately the same as those of chlorothiazide. However, it has the disadvantage that it must be given by injection.

The data of this study confirm the data of previous bioassay studies,[1-4] and demonstrate that orally administered chlorothiazide is more potent as a diuretic agent than intramuscularly administered mercaptomerin. The tendency of the two drugs to produce disturbances in serum biochemical architecture is roughly equal. A mild, clinically significant hypokalemia was observed in two of the 20 patients in this study, and one of these had cirrhosis and a poor nutritional status. It appears that if the patient has an adequate dietary protein intake and if the doses of chlorothiazide are sufficiently spaced (early morning and late afternoon), little difficulty in the way of production of hypokalemia is to be anticipated. By far the most common clinically important syndrome due to overenthusiastic diuretic therapy and rigid salt restriction is hypochloremic alkalosis, but this can be prevented by the concurrent use of ammonium chloride.

A second important observation in this study concerns the technic for observing comparative diuretic responses. When the patient becomes free of edema after the use of either chlorothiazide or mercaptomerin, sodium excretion may decrease. This indicates that the sodium stores of the body have been depleted. This study has demonstrated that when the body has been depleted of sodium and water by the administration of one diuretic, the response to the second diuretic (as under the conditions of this study) will be spuriously low if the body stores of sodium are not permitted to return to control levels before the second drug is administered. If this is not permitted, the difference in drug potency may be due to experimental design, rather than to the difference in the diuretics studied.[1] Furthermore, changes in body weight are more erratic or inconsistent than changes in urinary sodium. To satisfactorily evaluate the comparative potency of two or more diuretics, observations should include urinary volume and excretion of sodium, and the patients must receive an identical controlled intake of dietary sodium and distilled water.

Summary

Chlorothiazide (Diuril) administered orally has been found to be a somewhat more effective saluretic agent than mercaptomerin (Thiomerin) administered parenterally to 20 edematous patients. The side effects due to chlorothiazide have been found to be rather minimal. Mild hypokalemia occurred in two of the 20 patients, and was readily corrected. The most common electrolyte disturbance due to chlorothiazide (and mercaptomerin) therapy is hypochloremic alkalosis.

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CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Report of Case

A 34 year old white man, a custodial supervisor, was admitted to Hines Veterans Administration Hospital in 1952 because of hematemesis and melena of four weeks' duration. In the eight preceding years he had had four major episodes of hematemesis and melena, and about 15 barium-meal evaluations of the upper gastrointestinal tract and four esophagoscopic procedures had been done, as well as proctoscopic and barium-enema examinations. He said that for five years he had not ingested alcoholic beverages, and for two years he had maintained himself on a bland diet. He had mild abdominal pain in the spring and fall months.

He was well developed, slightly obese, and essentially healthy in appearance. Physical examination did not disclose any abnormality other than diminution in amplitude of the right patellar, abdominal and cremasteric reflexes. Results of proctoscopic, gastroscopic, barium-enema and small-bowel studies, as well as cholecystography, were considered normal. An x-ray series of the upper gastrointestinal tract was considered normal, with a suggestion of a hiatal hernia. The discharge diagnosis was recurrent upper gastrointestinal hemorrhage of unknown cause.

The patient was admitted to the hospital again in 1956 after having had tarry stools for two days. Physical findings were not abnormal. Gastric aspiration shortly after admission revealed a 4 plus benzidine reaction. A chest x-ray and an electrocardiogram were considered essentially normal. X-rays of the upper gastrointestinal tract disclosed old ulcer deformity of the duodenal bulb, but a crater was not visualized. Operation was suggested to the patient, but he declined. The discharge diagnosis was duodenal ulcer, resulting in upper gastrointestinal tract hemorrhage. Blood transfusions were not given.

The patient's third and final hospitalization began on February 1, 1957, when he complained of upper abdominal fullness and dark stools of two weeks' duration. He stated that he had maintained the therapeutic regimen of antacids, belladonna and bland diet. The sense of abdominal fullness seemed to occur principally at night and was relieved by sitting, standing and eructation. The patient was well developed and well nourished but no longer obese, and was anxious, nervous and pale. He complained of epigastric tenderness when the abdomen was examined.

Early in this period of hospitalization an x-ray was made of the left hip, which was painful, and was said to disclose osteoarthritis.

In the latter part of his hospital stay a chest x-ray revealed discoid atelectasis in the right lung and a K.U.B. film showed generalized distention of the entire gastrointestinal tract.

The clinical course lasted about five weeks. Apprehension, pallor, worry about weight loss, and diaphoresis were recorded repeatedly in the nursing notes. There was a persistent slight spiking febrile course, except during the second week, when exploratory laparotomy was performed. Eight blood infusions were given, most of them during the final week. In the fourth week, icterus was noted. Ascites was present in the last two and a half weeks, and it was at that time that the pain in the left hip was most noticeable. Petechiae and splenomegaly were noted in the 48 hours prior to death, which followed a sudden elevation of temperature to 105° F. on March 6, 1957.

Differential Diagnosis

DR. GIBBEL (chief of surgery, Veterans Administration Westside Hospital, Chicago): This man's problem began when he was 26 years old, with episodes of hematemesis and melena. In the eight years prior to his first admission to this hospital in 1952 he had four major episodes of upper gastrointestinal bleeding. He had mild abdominal pain in the spring and fall, which is consistent with an ulcer history. During the same eight year period he had some good x-ray therapy to his upper abdomen, because he had 15 upper gastrointestinal series and numerous barium enemas.

When he came into the hospital here for the first time, he was 34 years of age and had been having hematemesis and melena for four weeks. He exhibited none of the stigmata of cirrhosis, he did not have hemangioma, and there was nothing to suggest congenital or hereditary disease. The most likely diagnosis was peptic ulcer. Perhaps 80 per cent of ulcers in this age group would be duodenal, and the rest would be in the stomach or esophagus.

A gastrointestinal series suggested hiatal hernia. The patient was anemic, with a hemoglobin level of 12 gm. and an erythrocyte count of 3,800,000 (table 1). There is no reason to think there was an abnormality of the kidneys producing chronic azotemia. The leukocyte count was normal, and gastric analysis showed 52 degrees of free acid with a total of 74. This is reassuring to think of as an etiologic factor in the bleeding, helping to confirm the initial impression of peptic ulceration. Esophagoscopic examination should establish or rule out peptic esophagitis. On five occasions the stools were negative for occult blood. After a hemorrhage such as this patient had, and if the hematemesis and melena occurred immediately before his admission to the hospital, there should have been some occult blood in the stools for two or three weeks.

The patient did fairly well for four years, until 1956, when he was readmitted because he had tarry stools for two days. X-rays did not reveal a crater but indicated ulcer deformity. Liver function seems to have been fairly normal. In cases of upper gastrointestinal bleeding a BROMSULPHALEIN® test is a good indicator of liver function; the albumin-globulin ratio is a little more gross but, I think, good. Nonprotein nitrogen was normal, 36. Urine was normal. This time he had 4 plus stools on three occasions, which would indicate he was losing blood into his gastrointestinal tract. He declined operation and went to his home.

After about a year he was readmitted for the third and final period of hospitalization. He was 39 years old. He entered in February; ulcer activity is more manifest during the months of February and March. But his story was changed. He complained of abdominal fullness and dark stools for two weeks and also stated that the fullness was relieved at night by sitting, standing or eructation. This type of pain can go along with pyloric obstruction and with a distended stomach. Pancreatic disease may give the finding of pain relief by bending over.

The most striking feature of this final period of hospitalization was the "persistent slight spiking febrile course." He had a sedimentation rate of 32, which can occur with neoplasia as well as with infection. Albumin-globulin ratio was normal, and this tends to rule out multiple myeloma and some of the collagen diseases. About a year had elapsed, and he had had a change of symptoms.

TABLE 1

LABORATORY DATA

	1952	1956	1957			
			First week	*Second week*	*Third week*	*Fifth week*
Erythrocytes (millions)	3.8	4.3, 2.7, 4.5				3.0
Hemoglobin (grams)	12	13, 10, 13	11.5-12.5	14.5-11.5	11.5	9.5-11.5
Leukocytes	8500	9300; 10,500		7200, 9800		51,200
Polymorphonuclear cells	64	78				
Lymphocytes	31	22				
Eosinophils	5					
Sedimentation rate			32	34-47		
Bleeding time			Normal			
Coagulation time			Normal			
Albumin-globulin ratio		3.8-2.0	3.7-1.6			
Potassium (milliequivalents)						3.6
Nonprotein nitrogen (milligrams)		36				69
Carbon dioxide (milliequivalents)						16.9
Chloride (milliequivalents)						93
Sodium (milliequivalents)						133
Amylase	15		54			
Lipase	140					
Glucose	101					
Thymol turbidity			2			
Van den Bergh (milligrams)	<0.5		<0.15-<0.5			
Urine						
Specific gravity	1.016	1.010	1.005			1.010
Albumin	0	0	0			0
Sugar	0	0	0			0
Free gastric acid (degrees)	52					
Total gastric acid (degrees)	74					
Occult blood in stool	Negative 5 times	4+, 4+, 4+	4+, 4+			
Serologic test	Negative	Negative	Negative			

Exploratory laparotomy was done during the second week of hospitalization. After operation the spiking temperature continued, and there was general distention of the gastrointestinal tract and atelectasis of the right lung. During the final two weeks icterus developed, ascites was noted, and the hip pain became worse. Possibly he had an abscess in addition to the primary disease process.

This patient might have had a benign leiomyoma that became leiomyosarcoma. Most gastric polyps are associated with achlorhydria. Possibly he had a gastric polyp which became malignant. One of the malignant lymphomas is a possibility. He could have had one of the follicular lymphoblastomas, or Hodgkin's disease, or lymphosarcoma; these can produce gastrointestinal bleeding. I think he had a malignancy of the gastrointestinal tract, and I probably would bet on lymphosarcoma. He could have had an abscess secondary to a perforation of a malignancy of the stomach. I will suggest two diagnoses: malignancy in the stomach and terminal bacteremia, very likely secondary to pseudomembranous enterocolitis.

Radiologic Findings

DR. KIRSH (consultant, radiology): An x-ray taken in 1952 shows a well-formed stomach and duodenum. There is a miniature hiatal hernia which does not look like the kind of thing that would produce bleeding of any importance. A later x-ray shows the constriction and outpouching pseudodiverticulum due to an old ulcer. It does not look like a crater. I might call attention to a suggestion of thickened folds in the antrum on one of the scout films. We sometimes attribute this to antral gastritis, especially if there is reason to think

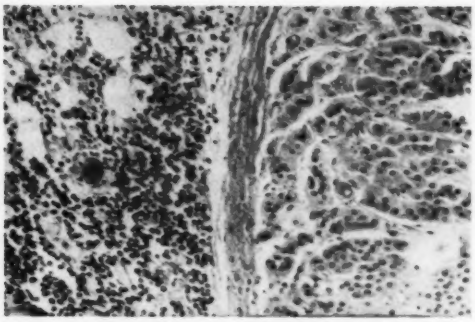

FIGURE 1. Infiltration of tumor submucosally showing a large mononuclear cell.

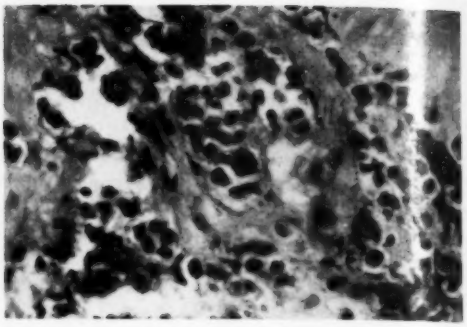

FIGURE 2. High-power view showing large mononuclear cells of highly malignant character.

there has been an ulcer. While lymphoma was suggested and while we sometimes diagnose this when there is very marked mucosal thickening, I do not think the appearance would justify this diagnosis.

Pathologic Findings

DR. RUBNITZ (chief of pathology): During the second week of the patient's final hospitalization a small biopsy specimen was taken from the wall of an infiltrating tumor of the stomach. The diagnosis was between lymphoma and small cell carcinoma. A reticulum stain was done, which offered no help. The histologic sections showed a diffuse infiltrate in the wall of the stomach, the cells appearing large and mononuclear. The exact derivation of these cells could not easily be determined, and the tissue was diagnosed as primary malignant tumor of the stomach, type undetermined.

The blood picture changed, the leukocyte count rising to over 50,000. The peripheral blood smear showed 65 per cent blast cells, a true leukemia picture, the type undetermined. Examination of the bone marrow showed it to be hypercellular, consisting almost entirely of blast cells. A final diagnosis of acute leukemia, undifferentiated type, was made.

On examination of the peripheral blood smear a clear distinction was noted between the lymphocytes and large mononuclear cells with vacuolated cytoplasm and a few small nucleoli. In the marrow replaced almost entirely by large blast cells, these cells demonstrated the vacuolated appearance with nucleoli like those seen in the peripheral blood smear.

At necropsy the peritoneal cavity contained over 2000 cc. of fluid. Subsequent microscopic examination of this fluid revealed large mononuclear cells with nucleoli. The heart showed only petechial hemorrhages, and the lungs minimal edema and congestion. The liver was approximately twice the normal size, weighing over 3000 gm. It was pale tan and fatty and there was no gross evidence of tumor involvement. The spleen was markedly enlarged, weighing 600 gm. No lymph nodes were found, and the pancreas was grossly normal.

The entire stomach was infiltrated by a thick fleshy mass which began at the esophagogastric junction and ended abruptly at the pylorus. There was no evidence of recent or old ulcer in the duodenum, but we may assume the patient did have a peptic ulcer at some previous time.

The sections of stomach viewed under low-power magnification showed an extensive infiltrate (figure 1) which on higher power revealed the large mononuclear cells (figure 2) such as were seen in the peripheral blood smear and in the bone marrow. Sections of bone containing bone marrow showed extensive infiltration (figure 3) by the same large mononuclear cells (figure 4).

In sections of liver there was a moderate amount of fat and more of the round cell infiltrates were noted. Similar infiltrates were found in the spleen, pancreas and retroperitoneal fat around, but not infiltrating, the adrenal glands.

FIGURE 3. View of bone marrow showing infiltration of malignant cells.

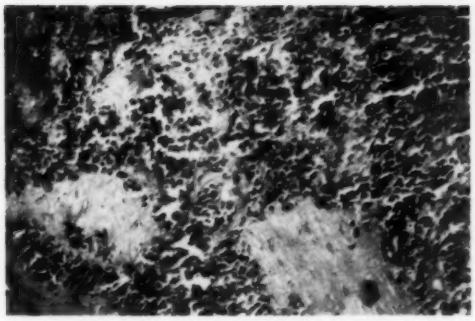

FIGURE 4. Higher-power view showing bone marrow infiltration of malignant lymphoma.

Discussion

Was this a case of lymphosarcoma of the stomach in which lymphatic leukemia developed, or was it a case of lymphosarcoma cell leukemia? Sternberg, who first described this condition, considered these cells in patients with lymphosarcoma to be *leukosarcoma* cells. He described the cells as being about 13.5 by 9 μ in size, approximately the size of the cells described in the peripheral blood and bone marrow smears and seen in the sections of stomach, liver, spleen, pancreas, and so on. He said the nucleus is oval or oblong, kidney-shaped and notched, and also said there is a single large, very prominent nucleolus. He described the leukocyte count as being up to 150,000 but usually lower; this patient's leukocyte count was about 50,000 at its peak. Sternberg stated that most of these originated in the anterior mediastinum but could occur with a primary lymphosarcoma in the gastrointestinal tract.

Gall and Mallory in their review of over 600 cases of lymphosarcoma stated that 50 patients or about 8 per cent had frank leukemia at one time or other during the course. Of these 50 patients, 13 were not leukemic when first observed and later became leukemic. These investigators found that most of these changes occurred following roentgen irradiation, while some developed spontaneously. Hauswirth and his group stated that a transformation from lymphosarcoma to leukemia occurred after x-ray therapy with surprising frequency. In studies using mice which had been implanted with lymphosarcoma it was found that lymphatic leukemia developed after irradiation. Recorded material was insufficient to prove that the x-ray is a causative factor in the transformation from lymphosarcoma to leukemia in human beings, but Hauswirth and associates said that such a relationship must be considered.

DR. KIRSH: This case was not a diagnostic triumph for the x-ray department, but it was a rather unusual case. I believe it is quite likely that the patient did have an ulcer, basing the belief on the radiologic findings. Of course there was also this tumor which was submucosal and was not identified. Another preamble I want to make is that only two of the gastrointestinal series were obtained at this hospital, the rest of them having been made elsewhere. This is not a criticism of the radiologists and the other doctors who ordered these gastrointestinal series. They faced a serious problem, that of a man with a great deal of bleeding, whose life was in danger and for whom a diagnosis was imperative; and, as we know, in the majority of cases a correct diagnosis can be made by x-ray. As to how much radiation this patient had received, I am unable to say.

When I came to Hines Hospital, about 10 years ago, I got hold of an ionization chamber and we measured the intensity of the dosage given to the skin of a patient in routine diagnostic x-ray procedures. It proved alarmingly high, and measures were instituted im-

mediately to reduce the dosage by placing aluminum filters in the machines and also by using cones to cut down the size of the beam. As a result, the doses were about one-fourth their original intensity, and we still are instituting measures to reduce them further.

In our gastrointestinal series there is a total of 13.7 r delivered, with the spot film, the fluoroscopy and the ordinary radiographs. For a barium enema the total is 3.9 r, for gallbladder study 6.4 r. Compare these amounts with a posteroanterior chest film which delivers 31 milliroentgens, and with the lateral chest film, 400 milliroentgens.

This is what we obtained here after instituting these measures to reduce the dosage. What was obtained elsewhere 8 or 10 years ago is debatable, and it is very likely that the amounts were much higher. Another thing to remember is that we stress a brief fluoroscopy here, and dependence on radiographs and spot films. The old teaching was to sit and observe the stomach fluoroscopically until one could make a decision as to the diagnosis. The modern trend is to take the films and get through, and if necessary make a second examination, rather than to fluoroscope until one has decided on the diagnosis.

I want to comment on the relation of leukemia to radiation. As Dr. Rubnitz mentioned, some experimental work has been done on animals which indicates a relationship; but lately there has been considerable discussion of x-ray and leukemia, and one of the important sets of data has been the research work done on the survivors of the Hiroshima and Nagasaki atom bomb explosions. An American Atomic Bomb Casualty Commission was established around 1950 to investigate the cases of leukemia that were discovered in 1948, 1949 and 1950 in these Japanese cities, three to five years after the bombings. A definite relationship was shown. There was an increased amount of leukemia among the exposed portions of the population, and it was shown that the closer to the center of the explosion the survivors had been, the more likely it was that leukemia would develop. This has been accepted as being meaningful.

Another significant report is that of the work of Court Brown and Doll on the incidence of leukemia among persons who have had x-ray therapy for rheumatoid spondylitis, which they call ankylosing spondylitis. They found a significant increase in the incidence of leukemia in this group. There also was some work done in Great Britain on the increased incidence of leukemia and of carcinoma of the thyroid in children who received irradiation of the thymus in infancy. You remember when it was fashionable to treat enlarged thymus, if it showed on the x-ray, with radiation therapy.

One other line of reasoning which is considered to be very suggestive is a study of the mortality rate of physicians. Shields Warren and others have made this study, based on the obituary columns of the *Journal of the American Medical Association*, and found that radiologists were about nine times as likely to have leukemia as people in general and that physicians as a whole had about twice the incidence of leukemia; of course we know that physicians other than radiologists often use x-ray.

All these lines of reasoning seem to be in agreement, and a biologist named Lewis came to the conclusion that they all show about the same likelihood of leukemia's following radiation. He figured out that it was between one and two times 10^{-6}, per rad, per year. The rad is an expression of the absorbed dose of radiation. Some of these statistics have been criticized and considered not too valid on the basis of the size of the sample. But the upshot of this kind of reasoning is that radiation is *not* innocuous; it may be very helpful in diagnosis, and we should use it when it is indicated. As a radiologist I tend to feel defensive about x-ray diagnosis, and I think it is unnecessary to point out to physicians that we have learned to value its contribution. So when an x-ray examination is indicated it should be pursued. The radiologist of course has the responsibility to hold down the dose as much as possible, and the referring doctor also has a responsibility to use it when it is indicated.

As to this particular case, I do not think anyone can say that radiation was an etiologic factor in the final disease; however, it is not impossible.

Management of Warts

Topical Medication

THEODORE CORNBLEET*

University of Illinois College of Medicine, Chicago

Surgery, Radiation, etc.

JOSEPH L. MORSE†

New York Medical College-Metropolitan Hospital Medical Center, New York

Statement by Dr. Cornbleet:

WARTS are common benign lesions of the skin caused by a virus infection. Their evolution and course are highly unpredictable, as spontaneous cures occur frequently and many warts can be eradicated by suggestion and psychotherapy. It is difficult to evaluate the true worth of any method of treatment, because it may be effective as a psychic factor only. Since time and simple measures will cure most warts, radical approaches should be reserved for special cases and resistant forms.

Verrucae differ only in appearance, which is largely a result of the accident of site. Experience shows that each type responds best to measures adapted to its size and to the number of lesions and the part involved. Therefore, it is convenient to consider the various types separately.

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THEODORE CORNBLEET

Verruca Vulgaris

Sessile in form, this variety commonly appears on hands and fingers. The lesions can be treated with trichloroacetic acid as a saturated solution in water, with care being taken not to spread the solution to the normal adjacent skin. A silver nitrate stick may be used in the same way, letting repeated applications accomplish the cure rather than using immediate rapid destruction, which often leads to unexpectedly exaggerated effects and to scarring. Meticulously careful application of a pointed carbon dioxide pencil for a minute under pressure may cause a blister after a day or two. The roof of the bulla with the wart at the center then may be pared away.

Liquid nitrogen is very effective. A mois-

tened swab applied accurately and with great care will cause the lesion to darken and blister after several hours; it then can be excised easily.

Periungual warts are especially difficult to manage; a 40 per cent salicylic plaster strip or patch, applied so it extends just beyond the edges of the lesion and kept in place for several days or a week, will soften the lesion so that it can be scraped. The plaster is then reapplied, and the same procedure is repeated until a cure is effected. Patience is often rewarded with favorable results, even in the presence of resistant periungual verrucae.

Flat Warts

Commonly found on the backs of children's hands and wrists and on their faces, these warts are the most amenable to suggestion. The lesions may be painted with Vleminckx's solution (liquor calcis sulfuratae N.F.) diluted with 15 parts water; the medicine should be freshly made each week. Administration of pills of 1 gr. mercury with chalk or 1/8 gr. mercury protiodide or 1 tablet BISTRIMATE® daily is sometimes effective.

Filiform Verrucae and Warts of the Bearded Area

These warts often respond to measures similar to those used to treat flat warts. A carbon dioxide pencil, judiciously used, is also helpful in these cases.

Plantar Warts

Warts of this variety present the greatest problem and are the most often incorrectly treated. In contrast to the experience of some physicians, I find it easier to cure the mosaic variety, with numerous tiny juxtaposed lesions covering areas of the soles, than to cure large deep verrucae at this site. A 40 per cent salicylic acid plaster applied for several days or a week softens the lesions. In most cases, the warts can easily be scraped away after one to three such applications; some are even lifted away with the dressing. Slight extension of the plaster's edge onto surrounding normal skin is not harmful. The larger lesions, usually numbering more than four, can be treated in the same manner, but the treatment, in my experience, is not as rapidly effective. If a persistent effort is made at each session to scrape away the softened keratinous material, most of these warts yield in time. At times, touching the softened wart surface with a silver nitrate pencil after removing the salicylic acid plaster will hasten the cure. However, one should rely more on patience and time than on attempts at deeper destruction by means of silver nitrate, nitric acid or other escharotics.

It is safe enough to entrust the plaster method to the intelligent patient who can be instructed in its use, thus relieving the physician of a long trial and usually producing favorable results. Only a few patients need radiation, surgery or deeply destructive therapy. A solid carbon dioxide crayon or liquid nitrogen on a cotton applicator may produce faster results. The carbon dioxide may be applied with pressure for a minute, and the liquid nitrogen momentarily with circumspection. The resulting blister holding the wart can be snipped away. Paring away the callused roof of the wart before applying these refrigerants facilitates their action. At the same time, greater care is then needed to prevent too profound destruction of the softened, bared tissues.

Summary

For the majority of warts, simple local measures used with patience and persistence and sometimes reinforced with oral medication and psychotherapy will produce a safe cure. Few warts require surgery, radiation or other drastic therapy.

Statement by Dr. Morse:

THERE is no uniformly successful specific treatment for warts. The method of therapy depends on the type of wart, its location, the age and psychologic status of the patient, and the cosmetic effect. Warts may disappear spontaneously or may respond to the mildest kind of treatment, or they may be so recalcitrant as to defy any method of treatment. In the ordinary, uncomplicated case, the simplest and least incapacitating form of therapy should be tried first.

JOSEPH L. MORSE

Warts are divided into four clinical types: (1) verruca vulgaris—the common wart; (2) verruca plana—the flat wart; (3) verruca plantaris—the plantar wart; and (4) verruca acuminata—the moist venereal wart. There are several varieties of the common wart including the digitate wart which occurs on the scalp, the filiform variety which appears on the neck and eyelids, and the periungual and subungual warts that develop around the nails.

In this paper, I will discuss the following methods of treatment: psychotherapy, internal remedies, injections, vaccines, electrosurgery, curettage and x-ray. The use of local applications, such as chemical caustics, solid carbon dioxide and liquid nitrogen, will not be considered.

The clinical observation that warts sometimes disappear after treatment with what is considered to be a placebo, e.g., after rubbing them with a potato or after other mystic procedures, led to the use of psychotherapy or suggestion therapy. Instances of intractable warts disappearing after suggestion under hypnosis have also been reported. Although psychotherapy does not give as high a percentage of cures as is obtained with actual destructive methods, it should be tried in certain cases, either when other methods cannot be used or when they have failed. In psychotherapy the patient is made to believe some treatment is really being used, and various forms of placebo therapy can be devised. Though it may be important to impress the patient with the fact that his warts will disappear, in considering the effect of suggestion therapy the possibility of their spontaneous disappearance should be remembered.

Internal remedies such as protiodide of mercury, bismuth, antibiotics, vitamin A, chlorpromazine and many other drugs have been used and at times are successful in treating the various types of warts. However, since no drugs have been shown to have a specific effect on the wart virus, their action is probably psychotherapeutic or the disappearance is spontaneous. In any event, one should be careful in using a potentially hazardous drug in treating a benign condition such as warts.

Vaccine therapy has been recommended, and its use may be considered when all other methods have failed. A phenolized, heat-killed suspension of warts has been employed, but has not proved to be of specific value. In fact, injections of distilled water have given as good results.

Treatment

Verruca vulgaris—Electrodesiccation with curettage is the method of choice for removing most common warts. If the patient has only a few warts and will allow local anesthesia, this is the quickest and surest method to destroy them. There is a possibility of scarring, but if the procedure is done gently with a minimal current there should be a good cosmetic result. If he has many warts, several of them can be treated at one time until all are removed. After the first treatment, however, it is best to wait before removing the remaining warts; in some cases when one or two warts are desiccated, the others disappear spontaneously. At times, slight trauma of any kind will cause a wart to disappear, and, on the other hand, they may recur after the most thorough removal.

Warts in the bearded region can be gently desiccated and curetted. When a very mild spark is used, local anesthesia is not necessary. However, one must be sure to remove all the warts, since any remaining ones may cause others to appear by auto-inoculation. Administering an antibiotic ointment may possibly prevent recurrences.

Periungual and subungual warts are difficult to remove and not uncommonly recur after electrodesiccation and curettage. This is often due to the fact that the wart extends under the nail, is therefore not entirely removed and regrows. To prevent this, as much as possible of the free nail near the wart should be cut away to expose the entire wart. Curettage must be thorough, but if there is a possibility of injury to the matrix of the nail elec-

trosurgery should not be undertaken. As a rule the latter is not recommended for treating warts around the nails. The conservative methods should be tried first.

Surgical excision of any type of wart is not recommended as there usually is scarring and the wart may recur in the scar. Scars, especially on the plantar surface, are painful and their presence makes further treatment of the recurrent wart very difficult.

In certain selected cases, low-voltage x-ray therapy is indicated in removing warts around the nails, especially when the conservative methods have failed. However, it should be given by a qualified dermatologist experienced in its use, and should never be given in excessive dosage.

Verruca plana—In removing flat warts, the use of psychotherapy and internal remedies is particularly indicated and gives a fairly high percentage of cures. In children, especially, this is the treatment of choice. External applications are also of value, and lotio alba U.S.P. in varying strength may be used for its peeling effect.

When psychotherapy and systemic remedies fail or when the patient desires immediate results, electrodesiccation is the method of choice. In most cases, an anesthetic is not used. Each wart is very mildly and superficially sparked and then gently scraped off with a skin curet. If the procedure is done carefully with a minimal current, there should be no scarring.

In some resistant cases of flat warts, very soft x-rays or grenz rays in small doses may be effective. They can be used in conjunction with psychotherapy.

Verruca plantaris—The plantar wart, especially the so-called mosaic type, can be most recalcitrant. The conservative methods of therapy are often successful, and psychotherapy alone or in conjunction with internal remedies should always be tried first. Vitamin A, bismuth given intramuscularly or by mouth, chlorpromazine, and other drugs have all been successful in a fairly good percentage of cases. Along with any treatment, orthopedic management is indicated. Pads, metatarsal bars and special shoes to avoid pressure are helpful.

Electrosurgical therapy is frequently used to remove plantar warts, but I do not recommend it, except as a last resort. It often causes painful scars and gives too high a percentage of failures and recurrences. If it is used, treatment should not be so radical as to cause a deep necrotic wound. Under local anesthesia the wart is moderately desiccated and removed *in toto* with sharp, curved scissors, care being taken not to injure the underlying fascia. Any remaining warty tissue can be gently curetted, but the base of the wound need not be desiccated. Bleeding can be stopped with gauze pressure. In the mosaic type, mild electrodesiccation and curettage may be successful.

X-ray therapy is the treatment of choice with many dermatologists, but some risk is involved and excessive doses should not be given. It may be employed in selected cases where the wart is very painful or the patient will not allow topical treatment, or both. X-ray therapy should not be used in removing the mosaic type of plantar wart.

Injection of 1 per cent NOVOCAIN® is successful at times in treating both the ordinary and mosaic types of plantar wart. It is indicated when there is a great amount of pain and discomfort. The method is not disabling and is especially convenient for multiple warts. The pain usually disappears in 24 hours, the wart softens and in a week can be lifted out with forceps.

Verruca acuminata—Psychotherapy with a mild topical treatment always should be tried first. Administering internal remedies has also been successful. If these fail, podophyllin is the treatment of choice.

In resistant cases, electrodesiccation and curettage may be necessary. This usually can be done under local anesthesia, but when there are many warts several sittings or a general anesthetic may be necessary. A vaginal and rectal examination should be done to rule out the presence of warts in these locations. Following operation, a weak potassium permanganate solution can be used in a wet dressing or a sitz bath. Chronic vaginal discharge or balanitis should be treated to prevent recurrences, and the patient's spouse should be examined for the possibility of transmission.

Summary

The management of warts is a problem: The physician must consider each patient individually and use his judgment to determine the best method of therapy. Conservative treatment gives a fairly high percentage of cures and should always be given a trial before radical destructive methods are used. Regardless of the form of therapy failures are not uncommon, and warts may recur after thorough removal. However, with persistence and therapeutic ingenuity they can be cured.

Comment by Dr. Cornbleet:

I agree with Dr. Morse that in curing warts (as anything else) one should favor the simpler and less destructive measures. Furthermore, I agree to the effectiveness, at times, of all the methods enumerated. However, perhaps there is room for a difference of opinion as to what should be emphasized.

My experience shows that recalcitrance of warts is in direct proportion to the age of the patient. Many warts clear spontaneously. Therefore, the older person with old verrucae either has less immunity to them, or his lesions are of a resistant and lingering nature. However, even warts which develop for the first time in the occasional individual in or past middle age show the same tendency to resist therapy. For these reasons I have found it rewarding to persist longer with simpler topical agents in children. On the other hand, in older adults, while I always start with topical remedies, it is a waste of time and effort to withhold more radical treatment very long.

I believe the most common error in the use of destructive measures for warts is the inclusion of too much normal tissue. As Dr. Morse said, the removal of one lesion often will lead to a happy result in accompanying, untreated ones. In the same way, it often suffices merely to sear the verrucal surface. Large, ugly, lifetime scars are too heavy a price for the removal of such benign lesions, especially in persons subject to keloids. Another caution is worthwhile: One should beware of deeply destructive treatment of warts about joints. I have seen unexpected, unfortunate sequelae occur at these sites. Something peculiar to the region of joints, probably their motion, exaggerates the effects of destructive measures.

Comment by Dr. Morse:

In my statement I did not discuss the use of topical remedies in managing warts, as that phase of the subject was to be considered by Dr. Cornbleet. However, I agree substantially with him that in most cases conservative topical treatment is successful if one has the patience and perseverance.

Although liquid nitrogen is effective in common warts, I prefer solid carbon dioxide (dry ice). It is more practical, easier to obtain, and less expensive. However, I use trichloroacetic acid in preference to dry ice for treating multiple warts. Its action may not be as rapid, but it is much easier to apply and less painful than solid carbon dioxide or liquid nitrogen.

I agree with Dr. Cornbleet that in plantar warts a combination of 40 per cent salicylic acid plaster and a chemical caustic is more effective than either one alone. I prefer trichloroacetic acid; but, regardless of the caustic used, paring of the macerated wart before each application is most important.

Dr. Cornbleet did not discuss the topical treatment of verruca acuminata. In this type of wart, when conservative procedures fail, the method of choice is to use a 20 per cent solution of podophyllin in tincture of benzoin applied only on the warts. A layer of VASELINE® will protect the surrounding skin from the liquid. In a few hours a reaction occurs, and the patient may take a lukewarm sitz bath to remove the podophyllin. The warts become necrotic and slough off in several days. After the reaction has completely subsided, it may be necessary to repeat the application.

I believe that in managing warts conservative methods should be tried first. Topical treatment is efficacious in most cases, and radical methods, such as surgery or x-ray, should be considered only after a thorough trial of other methods has proved ineffective.

Editorials

Postgraduate Medicine

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A DOCTOR AFIELD: HANS CAROSSA

HANS CAROSSA (1878 to 1956) is a celebrated German author. While he has been discussed in English literary publications and while some of his books have been used as texts in German classes in the British Isles, he is almost unknown in America, even though a number of his books are available in English as well as in Dutch, Danish, Finnish, Polish, Romanian, Swedish, Czech, Italian, Hungarian and French.

As an author Carossa never went far afield, since almost all his work is autobiographic. Thus, he is the only famous German writer who used his personal experience time and again as the main material of his stories. Unlike many physician-poets Carossa never gave up his practice during his long life. Most of his works, therefore, reflect his medical training. His Latin-sounding name is no literary pseudonym, but stems from his Roman ancestors. His great-grandfather came from Italy and had been a surgeon with Napoleon's armies. (We are told that he had an idea of the antiseptic treatment of wounds.) He followed the French armies and in 1817 settled in Bavaria. Carossa's father Karl was also a physician, with a number of publications to his credit in which he recommended the use of pilocarpine in the treatment of pulmonary diseases. This deserves to be mentioned, since Karl's famous son Hans also began to prescribe pilocarpine for his tuberculous patients soon after finishing his medical education in the universities of Munich, Würzburg and Leipzig. Like his father, Hans settled in Bavaria to practice medicine, but much to his father's concern he continued a most unhealthy interest in contemporary literary circles in Bavaria, particularly in Munich. His growing responsibilities as a physician did not prevent his writing and, indeed, publishing poems.

Carossa's early experiences with the ravages of tuberculosis find a very forceful expression in his first book, "Dr. Buerger," which was published before World War I, with a contemporary series of poems called "The Flight." In his later years Carossa rarely mentioned this edition and one has the impression from

In commemoration of the eightieth anniversary of the birth of Hans Carossa, December 15, 1958.

some of his comments that he would have preferred his readers to concentrate on his later books, of which two, "Roumanian Diary" and "Dr. Gion," have won the greatest fame. The "Roumanian Diary" is the poetic account of an army doctor (Carossa served as a physician with a Bavarian infantry unit) during World War I. In this book his motto and, indeed, a theme in most of his later writing is first set down. This phrase has become very well known, and Carossa's name is hardly ever mentioned without its being quoted: "Wrest the light from the jaws of the serpent."

"Dr. Gion" was published when Carossa was in his 40s. Again, it is not difficult to find the parallels between Carossa's life as a physician in a small southern German town and his "Dr. Gion." This book is a loosely knit and very sensitive story of the development of character and the growth of personalities of the main figure Dr. Gion and his patients and friends through mutual experiences.

This portrayal of the development of character under the molding influence of experience is one of Carossa's principal literary objectives. In his charming autobiographies, conscientiously covering his life from childhood to his early years as a physician, the reader will rediscover this theme many times. It must be Carossa's art of appealing to his readers' sense of or, perhaps, hope for morality which has won him such a wide audience in Europe. He imperceptibly reassures them that man is basically good and that, allowed to grow, he will become better. We may wish to flatter ourselves as physicians that this attitude of hopefulness has sprung from his profession and that his insistence that even bitter experiences bear a light for the one who can win it "from the serpent's jaws" stems from his wisdom as a doctor.

We must assume that Carossa's great success as a poet has to do with the qualities just mentioned rather than with his mastery of language, since his style and use of German were not original with him but were strongly influenced by Goethe, Hugo von Hofmannsthal, Stefan George and Rainer Maria Rilke, a fact which Carossa himself always acknowledged. Carossa did not develop a new philosophy and never delighted his readers with any unusual plot, yet he was a celebrated poet. When he died on September 12, 1956, in his obituary the London *Times* recalled some of the honors he had received, which included the Munich prize for poetry (1928), the Swiss Gottfried Keller prize (1931), and the Frankfurt Goethe prize (1938). His other distinctions included two honorary Doctor of Philosophy degrees, from the University of Cologne (1938) and the University of Munich (1948), and the Italian San Remo prize for literature.

In 1946 the Nobel laureate of literature, Hermann Hesse, considered suggesting Carossa for the Nobel prize.[1] However, he did not carry out his intentions. One must assume that Hesse feared at that time that Carossa's political attitudes were not generally fully understood. In the late 1930s Carossa had been present in the so-called Klosterhaus circle at Lippoldsberg, where a group of poets gathered around Hans Grimm. This group was believed to be tolerant of certain features of national socialism, and Carossa was attacked for his participation. However, a careful analysis of Carossa's work and his actions during World War II left no doubt as to the integrity of his political beliefs,[2] often professed without regard for his personal safety.

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MEDICAL AWARDS

Awards and prizes continue to multiply in the field of medicine as more and more organizations, agencies and philanthropists recognize the significance of such awards as a public relations mechanism. When an award is made, the publicity given to the citation calls attention to the good cause which is be-

ing served or which has been served, to the accomplishments of the person cited, and to the need for further progress.

Two recent awards are especially significant because of their unusual character. Mr. Basil O'Connor, president of the National Foundation for Infantile Paralysis, was granted this year the Lasker Award. His leadership in advancing investigation of infantile paralysis, in understanding the close relationship that prevails between education and progress in medicine, and in promoting the care of the sick has been recognized all over the world. The present award is notable as being the first made by the Lasker Award Committee to a person who is not a scientist, a physician or a professional writer, but who is definitely a talented administrator and leader.

A year ago the Association of American Medical Colleges created an annual Abraham Flexner Award for Distinguished Service to Medical Education and quite rightly presented Abraham Flexner with the first citation. A distinguished committee was created, consisting of two deans, two professors in the clinical sciences, and two professors in the basic sciences, to encourage nominations and consider the next person to receive this award. The person thus honored must be a teacher of note; a scientist; an investigator; a writer; an administrator; a conscientious citizen; a leader; a servant of his community, state and nation; a member and officer in learned societies; respected in academic halls and, perhaps, even in the chambers of Congress; a holder of responsible office in many organizations; and an inspiration to friendship and trust. Above all, he must be a person with vision, initiative and performance in his consecration to the welfare of medical education.

Obviously, the number of persons to meet these qualifications is not going to be great, yet the committee immediately found one man who qualified fully. The winner of the second Abraham Flexner Award is Dr. Joseph Clarence Hinsey, whose distinguished career has carried him through the faculties of Northwestern, Western Reserve, Washington and Stanford universities. He has been professor and head of the department of physiology and anatomy at Cornell University Medical School, dean and director of New York Hospital-Cornell Medical Center, member of the President's Commission on Medical Needs of the Nation and the boards of trustees of Memorial Hospital, Sloan-Kettering Institute, China Medical Board and Cornell University, contributor to and editor of scientific publications, and a member and officer in many learned societies. He is an expert in interpersonal relations, a special pleader in Washington for the cause of medical education, and is famous for his altruistic devotion to good works. In the Association of American Medical Colleges, Dr. Hinsey has been vice-president, president and chairman of the executive council during eight crucial years when his leadership was paramount to the growth in dimension and influence of the Association, both internally and throughout the nation and the world.

MORRIS FISHBEIN

ENCOURAGEMENT OF RESEARCH

In his autobiographic commentary on education and science, "The Natural History of a Savant," the great Professor Charles Richet indicates how necessary is adequate support of investigators so that they may pursue research without the distraction of earning a living. Richet is credited with the discovery of anaphylaxis, for which he received the Nobel prize in 1913. He observes:

"If we wish for progress, savants must be given means of working. Not only must they be assured of laboratories equipped with indispensable apparatus; but above all they must be assured, by suitable emoluments, of a livelihood. They must also be given assistants who are amply remunerated. In fact, scientific institutions must be created independent and autonomous, whose sole function will be the disinterested search for truth.

"Engineers, doctors, lawyers, professors, apothecaries, officers, bankers have professions which enable them to live. But, well informed as they are, they are not savants, for their calling absorbs the best part of their time.

They can therefore only work at science as something extra in their leisure moments.

"Now science demands exclusive sacrifice. It admits of no sharing. It requires from devoted individuals the consecration of their whole existence, their whole intelligence, their whole labour.

"Therefore, because of the inherent uncertainty of all research and the inability of this research to enrich its devotees, savants can only pursue their labours if they are given means of providing food and housing and also of supplying themselves with sufficient working instruments."

MORRIS FISHBEIN

ELECTRONIC TECHNICS IN MEDICINE AND BIOLOGY

AUTOMATION in medical and biologic research has advanced so far that annual conferences are now held to inform investigators of the rapid progress made in various institutes and universities. The eleventh annual conference was held in Minneapolis in November, under the chairmanship of Professor Otto H. Schmitt of the University of Minnesota. One manuscript concerned using electronic computers in medical diagnosis, leading to an understanding of probabilities by statistical analysis. Dr. Reginald G. Bickford of the Mayo Foundation discussed computational aspects of brain function. Similarly, the interpretation of electroencephalographic waves occupied a session, and a new method was proposed for analysis of electrocardiographic recording. Indeed, computers are now being applied in the study of human metabolism, respiratory infections, physiologic variables, muscle activity and blood flow. One proposal by Edward H. Hon of the department of obstetrics and gynecology at Yale University involved studying fetal heart-rate patterns during labor, with a view to finding some relationship to cerebral palsy, mental retardation and epilepsy when the fetus is in jeopardy.

The movements of the pupil of the eye are being determined by using electronic devices and relating changes in pupillary movements to conditions of disease that otherwise are not easily detected early in their course. Dr. Colin S. Pittendrigh of the department of biology at Princeton University reported on the oscillatory nature of physiologic processes. The human body has functions which are rhythmical over a period of 24 hours. The physiologic changes which are repetitive at about one day intervals and are called circadian rhythms were also discussed by Dr. Earl E. Bakken of the University of Minnesota Medical School.

New understanding of human physiology is coming from these studies which could not have been made satisfactorily before the development of new devices for infinitesimal measurements.

Among the various uses of electronic computers in medical diagnosis, Drs. Robert S. Ledley and Lee B. Lusted mentioned the possibility of listing symptoms and then, by accurate computing, determining the minimum number of additional tests for diagnosis.

Thus they said:

> The collection of statistics in order to generate the necessary probabilistic data of a realistic situation involving many diseases and symptoms is a data-processing problem to be handled by electronic computers. One technic is to make the computer behave like a conditional probability, or learning machine. The computer simply records the number of patients that have each of the symptom-disease complexes that actually occur. Thus the computer makes a continuing tally corresponding to each symptom-disease complex column described above. It then becomes a straightforward matter for the computer to generate the appropriate conditional probabilities from the data accumulated.

When the diagnosis is sufficiently accurate, the value of various forms of treatment associated with alternative diagnoses becomes a problem for consideration. Thus, "The determination of the appropriate value for a particular treatment-diagnosis combination, or the relative values of a particular treatment with respect to several possible diagnoses, can involve intangibles. For example, many such value judgments involve social, economic, ethical and moral considerations that are of great importance."

The use of computers is to aid, not replace, the physician. The computers may even complicate the physician's responsibilities, since he will have to learn more in order to employ and evaluate the procedures mentioned.

MORRIS FISHBEIN

MULTIPLE SCLEROSIS

FROM the National Multiple Sclerosis Society comes a special year-end report[1] of medical and scientific advances in the campaign against this dreadful disease. New technics in laboratory investigations are yielding observations of significance. By means of gas chromatography more rapid and precise analyses of blood lipids and fatty acids are now possible. These substances compose the layers of the myelin sheaths which are the center of attack in multiple sclerosis. Under a grant from the National Multiple Sclerosis Society, investigations by this technic are being made at the Sinai Hospital in Baltimore.

In Cincinnati, Dr. Albert B. Sabin is investigating the possible role in multiple sclerosis of the common virus which causes herpes simplex. He has found that this virus may lie dormant in the nervous system and be provoked into bouts of activity in which it may attack the glial cells that regulate the formation of the myelin sheath.

In new studies of the myelin sheath, x-ray diffraction and electromicroscopes are being employed. The neuroglial cells constitute 80 to 90 per cent of the cells of the central nervous system and play an important role in the formation and maintenance of myelin. At this time the National Multiple Sclerosis Society is sponsoring more than 30 different investigations from many different points of view and extensive studies also are being carried on under grants from the National Institutes of Health and other organizations. One study of some special interest is a current grant for investigating a possible genetic basis of multiple sclerosis in identical twins. Thus far a genetic factor of significance has not been found.

In the *British Medical Journal*, Dr. Michael Kremer,[2] who heads the department of nervous diseases in Middlesex Hospital, reviewed the current status of multiple sclerosis in Great Britain, where the disease affects about one of each 2000 of the population. He has analyzed the various methods of treatment, including the use of vaccines, pyrexia, vasodilators, steroids, arsenic and intraspinal therapy. After considering the effects of these methods, he says, "Whichever of these means of treatment is used, if the patient's mobility is affected, whether owing to disturbance of power, tone, coordination or sensation, then his re-education with the help of trained physiotherapists is an essential part of treatment. It is probable that at present this may well be the most important part of treatment, and it is clear that this calls for special training of physiotherapists and for their being part of a team engaged specially in helping such disorders of mobility and equilibrium. Unless the therapists know what they are trying to achieve and have adequate leadership, they may well share the hopelessness that is so frequently seen in those faced with these patients. It is remarkable how much an enthusiastic doctor or department can achieve in restoring really useful function, quite apart from the help that can be given by introducing mechanical aids in the kitchen, bathroom and elsewhere in the house."

At this time the treatment of multiple sclerosis is symptomatic. Because of the extent and variety of symptoms, complete care of such a patient requires most comprehensive therapy. An essential part of the treatment is still to maintain the morale of the patient and of his relatives at as high a level as possible. In the face of the progress and desperation of this disease, the attitude of the physician and of the nurses and attendants—in fact, of all who come in contact with the patient—is important in sustaining morale.

MORRIS FISHBEIN

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2. KREMER, M.: Drug treatment of disease: Disseminated sclerosis. Brit. M. J. 2:1463-64 (December 13) 1958.

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New *for your armamentarium*

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A

• MICROCHEMISTRY CENTRIFUGE

DESCRIPTION: Especially designed for microchemistry determinations, this unit features quick, efficient centrifugation at 13,500 rpm. Two sets of eight polyethylene adapters are furnished with each centrifuge to accommodate 1, 0.5 and 0.25 ml. glass and disposable plastic tubes. Sound is reduced by the precision machining and perfect balance of the head; shock-mounting of the housing, motor and head; and the separate ventilating systems for head and motor chambers, which also prevent overheating of the instrument and specimens. Safety is assured by the special cover for the angle head and the heavy-gauge steel centrifuge cover, which must be secured before the motor will start. Four rubber suction feet absorb vibration and prevent the machine from creeping. A dial timer may be set for 1 to 30 minutes; an automatic brake stops the head gradually in 60 seconds without disturbing the sediment.
PRODUCER: Clay-Adams, Inc., New York.

• TACE® (New Dosage Forms)

PURPOSE: Estrogen therapy.
COMPOSITION: Tace 25 mg.: Each tablet contains 25 mg. chlorotrianisene; Tace With Ergonovine: Each tablet contains 25 mg. chlorotrianisene and 0.1 mg. ergonovine maleate.
CAUTION: Because of its oxytocic action, Tace With Ergonovine should not be given before completion of the first stage of labor.
DOSAGE AND ADMINISTRATION: Tace 25 mg.: for postpartum breast engorgement, 2 capsules every six hours for six doses, beginning within eight hours after delivery; for menopause syndrome, 1 capsule daily for 30 days; for carcinoma of the prostate, 1 capsule daily. Tace With Ergonovine: for postpartum breast engorgement and uterine atony, 2 capsules every six hours for six doses, beginning within eight hours after delivery.
HOW SUPPLIED: Bottles of 12 and 60.
PRODUCER: William S. Merrell Co., Cincinnati.

• SUMYCIN® SYRUP AND AQUEOUS DROPS (New Dosage Forms)

PURPOSE: Broad-spectrum antibiotic.
HOW SUPPLIED: Sumycin Syrup: 60 cc. bottles; Sumycin Aqueous Drops: 10 cc. bottles with Flexidose dropper.
PRODUCER: E. R. Squibb & Sons, division of Olin Mathieson Chemical Corporation, New York.

(Continued on page A-118)

CHYMAR®

AQUEOUS is indicated as: # a therapeutic agent —Chymar abolishes inflammation, hastens absorption of edema and blood extravasates, relieves pain, restores impaired local blood and lymph circulation. # a prophylactic agent—Chymar, when given early, suppresses the development of the inflammatory tissue reaction and edema. # an adjunctive agent—Chymar supplements antibiotics in local infections and is useful in inflammatory dermatoses. # Supplied: 5 cc. multiple dose vials. Each ml. contains 5,000 Armour Units of chymotrypsin. Also available—Chymar in Oil.

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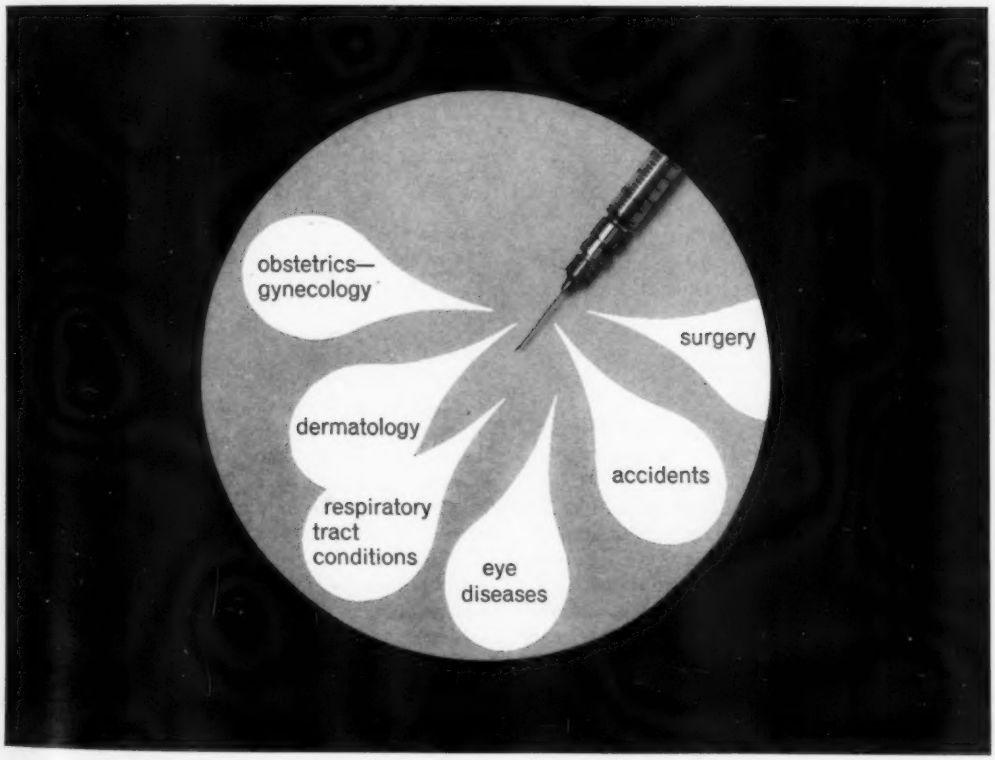

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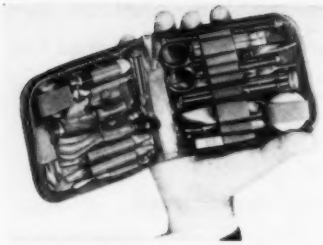


• MEDIKIT®

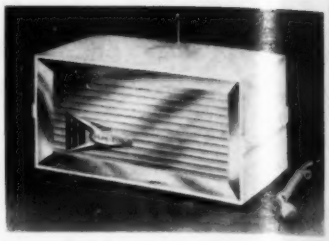
DESCRIPTION: Containing 24 essential diagnostic and therapeutic instruments and medications, this pocket-sized, full-grained top leather kit measures 5 by 4½ by ¾ in. and weighs 13½ oz.
PRODUCER: The Grant Company, Chicago.

• WHITE FEATHER DISPOSABLE NURSE'S CAP

DESCRIPTION: Resembling starched linen, this inexpensive cap may be discarded when soiled. Popular styles are available; other styles may be purchased by special order.
HOW SUPPLIED: Packages of five.
PRODUCER: R. J. S. Corporation, Detroit.

• CELGINACE AND COMBINACE

PURPOSE: To relieve constipation.
COMPOSITION: Celginace: dioctyl sodium sulfosuccinate (Colace) and calcium and sodium alginates; Combinace: PERI-COLACE® (Colace and Peristim) and calcium and sodium alginates.
DOSAGE AND ADMINISTRATION: 1 to 3 tablets daily.
HOW SUPPLIED: Tablets in bottles of 30, 60 and 250; granules in 147 and 294 gm. tins.
PRODUCER: Mead Johnson & Company, Evansville, Ind.



• HUMI-ZON® HUMIDIFIER

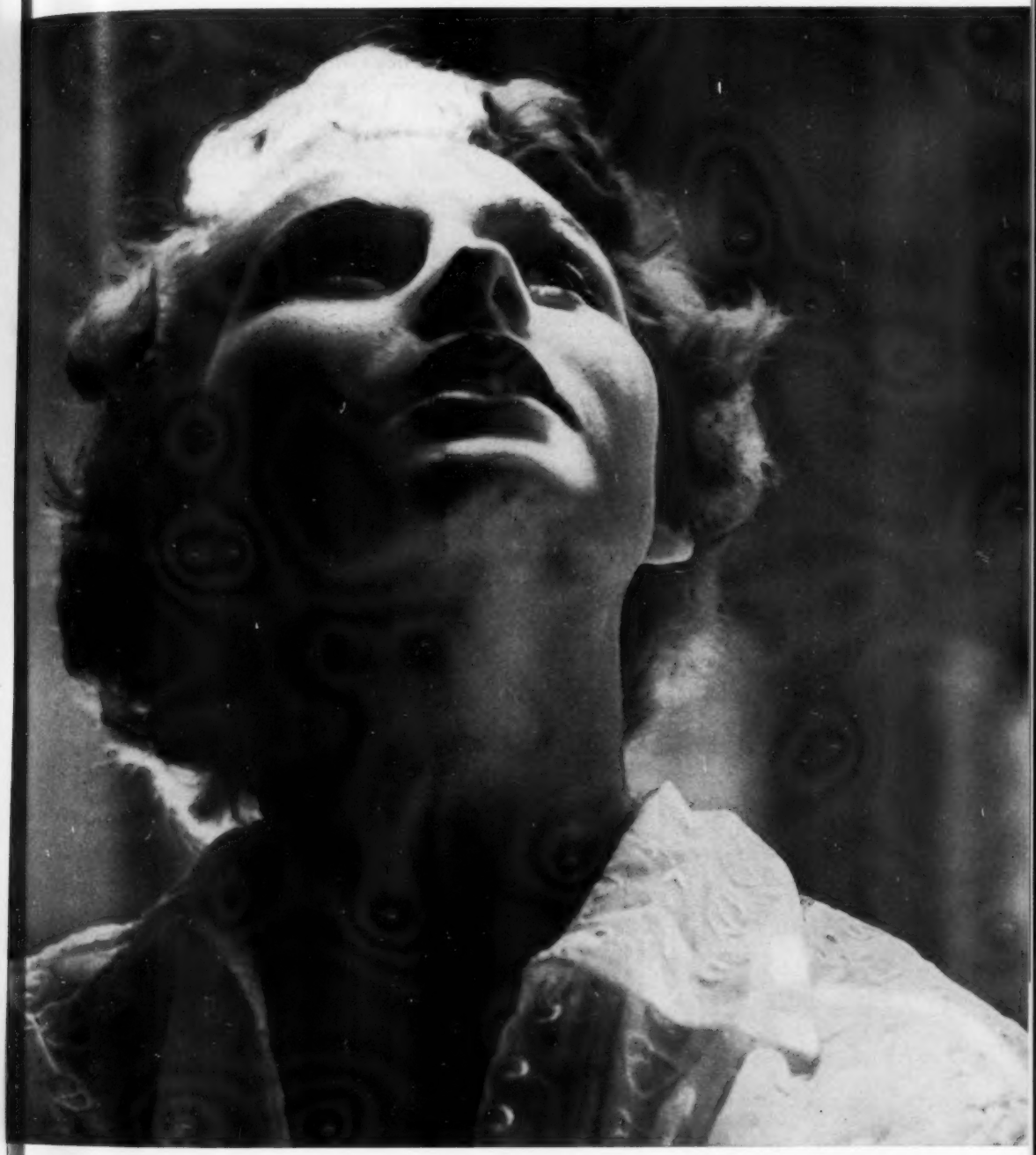
DESCRIPTION: Portable and self-regulating, this unit keeps humidity at 40 to 50 per cent in a room 10 by 14 by 8 ft. Room air is drawn through a removable, washable filter which screens out air-borne dirt, washed through a saturation chamber, and recirculated about the room. Approximately 2 lb. water is added to the air in a day. The unit is available in a 12 by 8 by 6 in. plastic cabinet in either turquoise or ivory with gold trim and grille.
PRODUCER: Safeguard Corporation, Lansdale, Pa.

• MOBILE CHAIR

DESCRIPTION: Highly maneuverable, this chair can be propelled by the user's pushing with one or both feet. Adjustable footrests and folding legrests can be attached or detached by push-button control. The frame is made of lightweight, chrome-plated tubular steel. Positive-locking wheel brakes may be purchased as extra equipment. A commode-type chair with a removable vitreous enamel pan is also available. The hardwood slip seat slides from the rear to expose the commode seat. All models are equipped with ball-bearing swivel casters with 5 in. gray, nonmarking rubber tires.
PRODUCER: Colson Corporation, Jonesboro, Ark.

(Continued on page A-120)

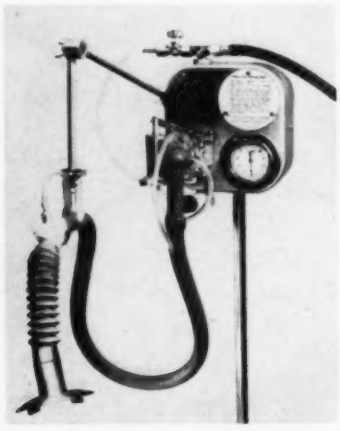
r your ambulant asthmatic . . . **"Air in a hurry!"**



Nephenalin®, the square purple tablet that relieves asthma with nebulizer speed for 4 full hours, offers convenience and reassurance to your ambulant asthmatic patient. Placed under the tongue, the NEPHENALIN tablet quickly releases 10 mg. of Isoproterenol HCl, the potent homologue of epinephrine, for immediate opening of the airway. Swallowed, the NEPHENALIN tablet provides theophylline (2 gr.), ephedrine (3/8 gr.) and phenobarbital (1/8 gr.), for sustained protection from asthmatic seizure. NEPHENALIN is available for your prescription in bottles of 50 and 100 tablets. Also available: NEPHENALIN PEDIATRIC. *Thos. Leeming & Co. Inc.* NEW YORK 17, N.Y.

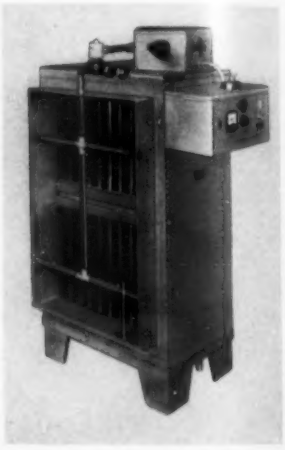
• CARDI-ALL ELECTROCARDIOGRAPH
(Fleetwood Model)

DESCRIPTION: The two speed mechanism of this direct-writing portable instrument allows instantaneous change from 25 to 50 mm. per second. The complete selection of leads includes the standard limb, Goldberger, Wilson chest and conventional chest. Leads may be changed without shutting off the motor. The unit uses full-width waterproof paper and either a standard-width or thin-width stylus which cannot burn out. The cabinet is available in blond or natural solid mahogany.
PRODUCER: Beck-Lee Corporation, Chicago.



• DOTCO RATE CONTROL ATTACHMENT

DESCRIPTION: For use with the Dotco Respirator or Deep Breather, this unit is adjusted to cycle at a slower than normal breathing rate. It initiates a breathing cycle if the patient does not make a breathing effort within the adjusted time cycle. For the apneic patient, the attachment provides time-cycled, pressure-limited controlled respiration. On any breathing effort of the patient, the time cycle is canceled and the breathing pattern is followed.
PRODUCER: Ohio Chemical & Surgical Equipment Co. (a division of Air Reduction Company, Inc.), Madison, Wis.



• AIR CLEANER
(Series 300)

DESCRIPTION: This unit has been reduced in size by one-fourth, facilitating installation and maintenance. The ionizing-collecting cell, a new design, maintains the balance between voltage and spacing in the collecting-plate section. An "inside curve" on the face of the negative electrodes provides a maximal area of electron discharge. Plate spacing has been reduced by 5/16 in. to increase intensity of the electrostatic field between the collecting plates.
PRODUCER: Electro-air Cleaner Company, Inc., McKees Rocks, Pa.

• CHART DIVIDERS

DESCRIPTION: Available in sets of nine, these dividers have colored plastic tabs labeled for specific types of medical records, thereby facilitating location of records by either color or name. Each set of dividers, arranged in the standard order for patients' records, is made to fit chart holders, and can be punched to fit other types of holders.
PRODUCER: Physicians' Record Co., Chicago.

(Continued on page A-122)

NEW THERAPEUTIC CHEMICAL IN CONSTIPATION

Calcium Bis-(Dioctyl Sulfosuccinate)

The discovery by Wilson and Dickinson[1] at the University of Michigan that dioctyl sodium sulfosuccinate could correct constipation through fecal softening action marked a real advance in therapy. In cases of unimpaired bowel motility this new physico-chemical principle presented a new means of correcting bowel dysfunction without the need of catharsis.

Continuing research has now led to the development of a new therapeutic surfactant with more than double the surfactant effectiveness of the original dioctyl sodium sulfosuccinate.

This new substance, calcium bis-(dioctyl sulfosuccinate), reduces interfacial tension to a minimal value at a concentration of only 0.035 per cent. A minimal value of this order in dynes per centimeter requires 0.1 per cent or more of the older dioctyl sodium sulfosuccinate.

INTERFACIAL TENSION (Oil-Water Interface) *Calcium Bis-(Dioctyl Sulfosuccinate)*	
Dynes/cm.	**Concentration**
55.0	0.00%
13.3	0.01%
9.9	0.02%
8.4	0.03%
7.4	0.035%

Improved homogenization of the immiscible lipoid and aqueous phases of the intestinal content depends upon maximum reduction of interfacial tension. The greatest degree of fecal softening is achieved with surfactant agents capable of reducing interfacial tension to minimal values. Calcium bis-(dioctyl sulfosuccinate) represents a markedly more effective surfactant agent since maximum surfactancy results from less than half the concentration of previously used surfactants.

DOSAGE:

DOXICAL 240 mg. SOFT GELATIN CAPSULES — *for adults, one daily.*

DOXICAL 50 mg. SOFT GELATIN CAPSULES — *for children and adults with minimum needs, one to three daily.*

1. Wilson, J. L., and Dickinson, D. G.: J.A.M.A. 158:261-263 (May 28) 1955.

This new chemical, definitely superior in surfactant action, is indicated in the treatment of chronic constipation where non-laxative fecal softening therapy is the preferred regimen.

The usual adult dose is 240 mg. daily. For children and adults with minimum needs, 50 to 150 mg. daily may be given.

DOXICAL

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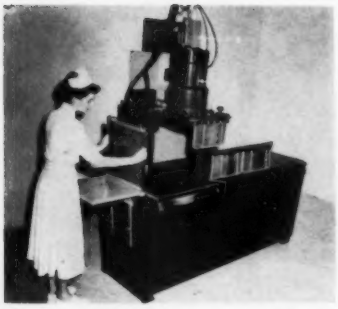


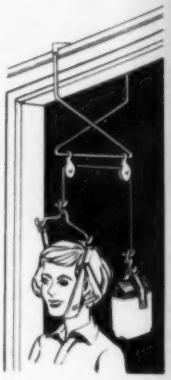
• X-RAY IMAGE AMPLIFIER

DESCRIPTION: The image reproduced on the 41 sq. in. pickup screen of this amplifier is at least 350 times brighter than that of a fluoroscope. The device permits the visualization of the entire pulsing adult heart and the complete stomach or colon while barium is being introduced. Deep tissues of the body can be studied in detail. The equipment housing the image tube, developed by the Picker X-Ray Corporation, is sufficiently flexible to allow the patient to be examined in almost any position. A closed-circuit television chain may be linked to the x-ray equipment.
PRODUCER: Rauland Corp., subsidiary of Zenith Radio Corporation, Chicago.

• JEFFERSON VENTILATOR (Model AC-6)

DESCRIPTION: For use during general anesthesia, this unit combines the four most important functions of mechanical ventilation and provides either pressure-limited or volume-limited ventilation. When the anesthetized patient is breathing spontaneously, the instrument acts as an assister, precisely following the pattern of respiration. The sensitivity is not affected by high gas flows. If the patient stops breathing, the ventilator automatically becomes a controller, filling and emptying the lungs at the rate, phase, pressure or volume set by the anesthesiologist. With the patient's first spontaneous breath it resumes the assister role. When the instrument is used as a controller, any breathing curve can be obtained. It may also be set as an absolute controller, time-cycled independently of the patient. When used as a controller with the optional nonrebreathing head, it provides mechanical, alternating positive-negative pressure ventilation during nonrebreathing (open-circuit) anesthesia, respiration or resuscitation.
PRODUCER: Air-Shields, Inc., Hatboro, Pa.

• OVERHEAD TRACTION SET

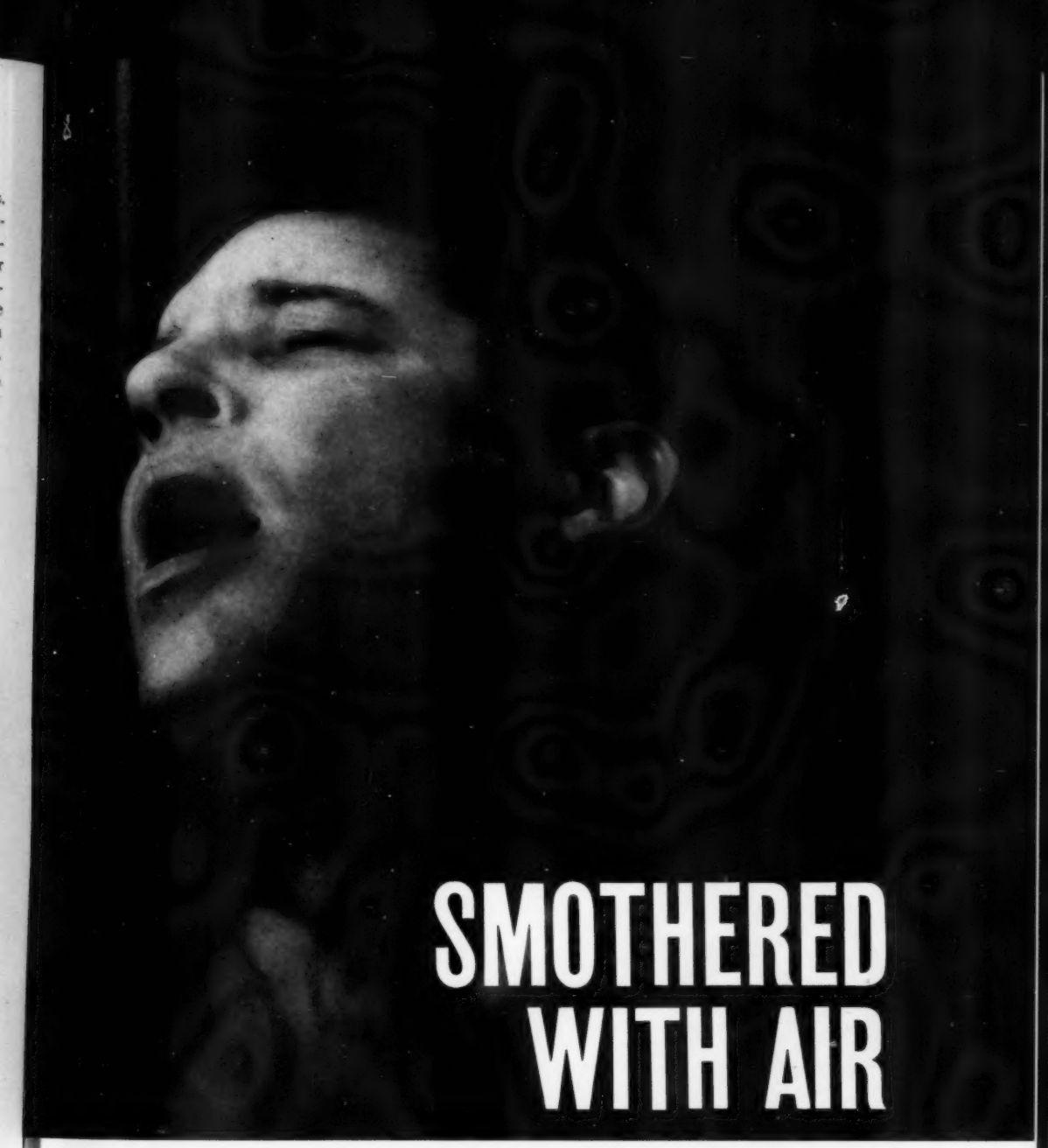


DESCRIPTION: Recommended for various conditions of the cervical area, this easily managed device of maximal weight provides comfortable positive support. The head halter, made of FABRICUSHION® foam rubber laminated with flannel, conforms to chin and facial configurations and requires only initial adjustment. The unit fastens to the top of the doorjamb and can be slid aside when not in use.
PRODUCER: The Akron Truss Company, Inc., Cuyahoga Falls, Ohio.

• PROTEF RECTAL SUPPOSITORIES

PURPOSE: Steroid and antibiotic therapy.
COMPOSITION: Each suppository contains 15 mg. hydrocortisone acetate and 15 mg. neomycin sulfate in water-miscible base.
CAUTION: Should be used with caution in patients receiving additional adrenosteroid therapy.
DOSAGE AND ADMINISTRATION: 1 suppository two to four times daily.
HOW SUPPLIED: Individually wrapped, in plastic boxes.
PRODUCER: The Upjohn Company, Kalamazoo, Mich.

(Continued on page A-124)



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• PULSE RATE COMPUTER (Model 120)

DESCRIPTION: Unit has a clip-on earpiece to monitor pulse rate, which is instantaneously recorded on a numerical indicator that can be read at a distance. It is not affected by interference caused by patient movement or electrosurgical and x-ray equipment. A caster-equipped stand permits the instrument to be located above the 5 ft. level. Attachments are available for pulse pickup from finger ECG leads and blood pressure cuff.
PRODUCER: Gilford Instrument Laboratories, Inc., Elyria, Ohio.

• ATRONIC PACER

PURPOSE: To provide direct internal cardiac stimulation and monitor heart action.
DESCRIPTION: A flexible insulated wire, ⅓ mm. in diameter, is enclosed in a needle of ½ mm. diameter and passed through the chest wall. The wire pierces the myocardium and can be left in place for long periods without damaging heart muscle. During insertion the electrode may be guided by either the monitor or lead test function. When the wire reaches the myocardium, impedance drops below the threshold level, indicating proper contact. Despite a wide range of impedances, the pacer delivers the current indicated on the current knob. The monitor indicates polarity and rate of the PQRS wave and is useful as an electrocardiograph. The unit is enclosed in a leather case, equipped with transistors, and weighs 1½ lb.
PRODUCER: Atronic Products, Inc., Bala-Cynwyd, Pa.

• WATERPROOF BLOOMERS

DESCRIPTION: Easily sponged clean, these bloomers are full cut, with waterproof elastic waist and leg bands for a comfortable and secure fit. Available in small, medium and large sizes, the bloomers are made of white plastic (model 99) or latex (model 4199).
PRODUCER: The Akron Truss Company, Inc., Cuyahoga Falls, Ohio.

• ORABILEX

PURPOSE: Cholecystographic medium.
COMPOSITION: Each capsule contains 0.75 gm. 3(3-butyrylamino-2, 4, 6-tri-iodophenyl)-2-ethyl sodium acrylate.
DOSAGE AND ADMINISTRATION: For adults, 6 capsules administered orally approximately 12 to 14 hours before examination.
HOW SUPPLIED: Envelopes of 6 capsules in boxes of 5, 25 and 100 and bottles of 250 capsules.
PRODUCER: E. Fougera & Company, Inc., Hicksville, N.Y.

The results of administering Delalutin before the 12th week of gestation to 82 women with habitual abortion were reported recently by Reifenstein.[1] Every patient had experienced at least three consecutive abortions immediately preceding the treated pregnancy. More than 68% of these women were delivered successfully and uneventfully following Delalutin therapy.

Boschann,[2] in a study of pregnancies with threatened abortion, found that:

37% of 73 pregnancies were carried to term without progestational therapy
64% of 42 pregnancies were salvaged by progesterone
83% of 73 pregnancies were salvaged by Delalutin

Eichner,[3] found that with Delalutin fetal salvage of infants below term weight (1000 to 2000 gm.) was significantly improved.
108 (76%) of 142 babies of this birth weight survived without progestational therapy.
16 (100%) of 16 babies of this birth weight survived with Delalutin therapy.
A comparison study was made of a group of repeated aborters treated with Delalutin, and a group with a similar history treated with bed rest and sedation.[4] Pregnancy salvage with Delalutin was twice that of the control group. Delalutin was found to be "highly active", well-tolerated and long-acting.

Delalutin offers these advantages over other progestational agents:

- longer-acting and more sustained therapy
- more effective in producing and maintaining a completely matured secretory endometrium
- no androgenic effect
- more concentrated solution requires injection of less vehicle
- unusually well-tolerated, even in large doses
- requires fewer injections
- low viscosity makes administration easier

DELALUTIN is also potent and safe therapy for: threatened abortion; postpartum after-pains; amenorrhea, primary and secondary; dysfunctional uterine bleeding not associated with genital malignancy; infertility with inadequate corpus luteum function; production of secretory endometrium and desquamation during estrogen therapy; premenstrual tension; dysmenorrhea; cyclomastopathy, mastodynia, adenosis and chronic cystic mastitis.

Administration and Dosage: Because of its low viscosity, Delalutin may be administered with a small gauge needle (deep intragluteal injection). Complete information on administration and dosage is supplied in the package insert.

Supply: Delalutin is available in vials of 2 and 10 cc., each cc. containing 125 mg. of hydroxyprogesterone caproate in sesame oil, and benzyl benzoate.

References: 1. Reifenstein, E. C., Jr.: *Annals N. Y. Acad. Sci.* 71:762 (July 30) 1958. 2. Boschann, H-W.: *ibid.*, p. 727. 3. Eichner, E.: *ibid.*, p. 787. 4. Hodgkinson, C. P.; Igna, E. J., and Bukeavich, A. P.: *Am. J. Obst. and Gyn.* 76:279, 1958.

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THE MEDICAL *Bookman*

► PRACTICAL LEADS TO PUZZLING DIAGNOSES

By Walter C. Alvarez, M.D., Professor Emeritus of Medicine, Mayo Foundation, Rochester, Minnesota. 490 pages. 1958, J. B. Lippincott Company, Philadelphia and Montreal. $9.00.

Written in the clear and easy Alvarez style, this volume contains many case histories from his years of practice and observation, which help to emphasize important points. He discusses the equivalents of psychosis and alcoholism, variants and equivalents of epilepsy, classifications of neuroses and psychoses, and the psychotic patient who loves operations. The chapter on "The art of handling nervous persons" should be read by all physicians. In addition, there is an excellent bibliography.

Since approximately 25 per cent of the patients seen by the family physician need some type of "simple psychosomatic care" to help them with their problems, this book may aid in better understanding and in more proper diagnosis of symptoms and complaints.

I. P. F.

► SYSTEM OF OPHTHALMOLOGY: THE EYE IN EVOLUTION

By Sir Stewart Duke-Elder, M.D., Institute of Ophthalmology, London, England. Vol. 1. 843 pages with 902 illustrations, 15 color plates and 350 marginal illustrations. 1958, The C. V. Mosby Company, St. Louis. $27.50.

This is the first of a proposed series of 15 volumes intended to supersede the "Textbook of Ophthalmology" by the same author. Although this work was written by Sir Stewart, the remaining volumes in the series will be rewritten in collaboration with his colleagues at the Institute of Ophthalmology.

The subject matter of this text is a comprehensive coverage of biologic knowledge of the basic science of vision, beginning with the responses of organisms to light, photosynthesis, and the effect of light on metabolism and movement. In part 2 the author considers the evolution of the visual apparatus in invertebrates, vertebrates, fish, reptiles and mammals. Part 3 is concerned with the function of animals' eyes, the vision of vertebrates, and the perception of light, color, form and space. Part 4 is a discussion of median and rudimentary eyes and luminous and electric organs.

The biologic study of the development of visual organs has been a major study in the basic sciences. Thousands of species of animal life have been studied meticulously from a number of standpoints, and it is not strange that most of our knowledge of the evolution of the processes of seeing came through scientists who were not trained in the field of medicine. The references at the end of each chapter are predominantly German and French; they date from the early part of the nineteenth century and refer to academic publications.

This book is interesting to today's ophthalmologist for several reasons: Such a background in biology appeals to the scientific part of his ego; it is the chief interest in a highly specialized field of medicine and is a most engaging topic for curiosity seekers. That Sir Stewart Duke-Elder wrote the book is another reason that ev-

(Continued on page A-156)

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ery ophthalmologist should read it. Finally, the volume will appeal to the science student as an example of the art of teaching basic sciences that have a practical clinical significance.

W. L. B.

► THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY (1958-1959)

Edited by J. P. Greenhill, M.D., Professor of Gynecology, Cook County Graduate School of Medicine, Chicago. 607 pages with 49 illustrations. 1958, The Year Book Publishers, Inc., Chicago. $7.50.

The thumbnail sketches in this volume of some of the most significant world-wide advances in obstetrics and gynecology include succinct descriptions of new diagnostic and therapeutic procedures applicable to the type of cases most frequently seen in practice.

In addition to the abstracts, the text includes editorial comments which in themselves make the purchase of the book worthwhile. It also contains a quiz which stresses some of the most fundamental points of the procedures mentioned throughout the volume.

E. A. B.

► CLINICAL ENZYMOLOGY

Edited by Gustav J. Martin, Sc.D., Research Director, The National Drug Company, Philadelphia. 241 pages, illustrated. 1958, Little, Brown & Company, Boston. $6.00.

The editor and five other investigators who are active in the field of enzymology have presented a timely and thought-provoking discussion of enzymes and their application to medical practice. Because the branch of clinical medicine concerned with the use of enzymes is expanding and maturing, it is appropriate that the present knowledge of the field be assembled.

This well-written volume introduces the uninitiated gradually into the field. The basic principles essential to understanding the biochemistry of the clinically used enzymes are outlined. A section on the enzymes used in medicine surveys the current status of the clinical work. The concept of biology presented is considered essential to extending efforts in medical enzymology.

In the chapter on protein biology, it is noted that, although the idea of clinical enzymology is not new, a general reluctance to accept innovation has retarded the therapeutic use of enzymes. The intricate complexity of protein structure and the relationship of enzymes and proteins are discussed. It is emphasized that the most fruitful study of enzymes can be derived only from their consideration in the milieu of the living cell and that the knowledge of enzymes and their actions can be best assimilated when viewed within a framework of biologic relativity.

The chapter on the chemistry of enzymes presents pertinent information on trypsin, chymotrypsin, ribonuclease, cholinesterase and hyaluronidase. Enzyme kinetics are not discussed in detail, but sufficient theory is included to permit an understanding of the essential features of enzyme reactions.

The discussion on the biochemistry of enzymes that are actually in clinical use or for which evidence exists for potential clinical utility concludes the laboratory science phase of the text.

In the following section on the current status in medicine of parenterally administered enzymes, it is noted that although the therapeutic efficacy of proteolytic enzymes is well established, much additional clinical investigation is needed to define specifically certain aspects of and indications for their use. The buccal and topical routes of administration are also briefly discussed.

A chapter on the diagnostic use of the enzymes provides a compact review of the subject.

Macromolecules, which are the essential ingredient of living matter, and the polymerizing systems involved in their synthesis are presented.

The concluding chapter on recapitulation and perspectives for clinical enzymology reviews the clinical application of trypsin and considers the potential application of three other enzymes: elastase in cases of arteriosclerosis, collagenase in the collagen diseases, and ribonuclease in certain types of cancer.

In the summation an attempt is made to incorporate clinical enzymology as a natural philosophy. The four dimensions characterizing macromolecules and the need to examine their actions in the light of statistical concepts are re-emphasized. Attention is focused on the polymerase-depolymerase systems as holding the delicately balanced key to health and sickness and to life and death.

J. M. M.

(Continued on page A-158)

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► THE PSYCHOLOGY OF MEDICAL PRACTICE

By Marc H. Hollender, M.D., Professor and Chairman, Department of Psychiatry, State University of New York, Upstate Medical Center, Syracuse. 276 pages. 1958, W. B. Saunders Company, Philadelphia and London. $6.50.

Dr. Hollender gives innumerable practical hints on the interpersonal relationships between doctor and patient in the practice of medicine. The advice is sound and exceedingly needful since most physicians learn these technics only by the system of trial and error and, frequently, at the cost of the patient's confidence.

Some of the most debated questions concern what to tell the person with cancer and what to tell his family and what to tell the woman who is going to have a baby, because she is not always happy. Although the author covers the whole gamut of problems that constantly arise in medical practice, he has in no sense of the word written a reference book but one that should be read and pondered and reread.

M. F.

► THE YEAR BOOK OF GENERAL SURGERY (1958-1959)

Edited by Michael E. De Bakey, M.D., Professor and Chairman, Department of Surgery, Baylor University College of Medicine, Houston. 588 pages with 149 illustrations. 1958, The Year Book Publishers, Inc., Chicago. $7.50.

In an editorial in a surgical journal, comments were made on the impossibility of reading through the many articles published to separate the worthwhile ones from the "trash." This is precisely what has been done in this volume. Worthwhile articles published in the year since the last edition of this book appeared have been abstracted and in some instances have been commented on by the editor.

A rapid perusal of the book indicates the ever-shifting emphasis in present-day surgery. In this edition, greater stress has been placed on procedures such as homotransplantation and cardiovascular surgery.

The major sections of the text are on shock, fluid and electrolytes, wound healing and neoplasms, with subdivisions on the head and neck, lungs and pleura, and other regions of the body. Twenty per cent of the book is devoted to anesthesia. The abstracts emphasize treatment and results and usually include statistical data.

That the nature of articles appearing in surgical journals is changing is indicated by the 52 reviews in the section on the heart and by the 40 reviews, mainly from the American literature, in the section on the lungs and pleura. In sharp contrast, only one article on the vermiform appendix is reviewed. To some extent, the interests of the editor will influence the articles selected, but certainly there can be no question that this text emphasizes the newer and more aggressive aspects of surgery.

Y. S.

► CLINICAL RADIOLOGY OF ACUTE ABDOMINAL DISORDERS

By Bernard S. Epstein, M.D., Chief, Department of Radiology, The Long Island Jewish Hospital, New Hyde Park, New York. 352 pages with 224 illustrations. 1958, Lea & Febiger, Philadelphia. $15.00.

The title of this book is somewhat misleading since Dr. Epstein, who has made many contributions to the radiologic literature, has actually covered most well-known acute, subacute and chronic intra-abdominal diseases which have x-ray manifestations.

The text is divided into four sections, the first covering congenital disorders and including most of the entities related to the congenital malformations seen primarily in pediatric radiology. Following is a discussion on neoplastic diseases, including extra-intestinal tumors and cysts. The third section is on inflammatory and vascular disorders, parasitic and granulomatous diseases and collagen and metabolic disturbances. The concluding discussion deals with traumatic disorders, foreign bodies and the effects of drugs.

Despite the relatively small size of the book, the coverage of abdominal disorders is quite complete. The discussions are concise but adequate and are followed by references to additional reading. The illustrations are well reproduced and plentiful. Unlike similar books, this text contains current material and may be used as a quick reference source for roentgenographic problems in abdominal diseases.

S. B. F.

(Continued on page A-160)

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► CEREBRAL VASCULAR DISEASES

By Irving S. Wright, M.D., Professor of Clinical Medicine, Cornell University Medical College, New York, and Clark H. Millikan, M.D., Consultant in Neurology, Mayo Clinic, Rochester, Minnesota, with 38 contributors. Transactions of the second conference held under the auspices of the American Heart Association, New York. 224 pages. 1958, Grune & Stratton, Inc., New York and London. $4.00.

As may be expected from its origin, this book is a mixture of investigative data, clinical material, new proposals, ideas pro and con and considerable candid comment and discussion on cerebrovascular disease. For the reader who desires practical material on the management of clinical problems, this text is impractical and almost exasperating at times, since much of the material is theoretical and controversial; but for the physician who wants a front-line view of the thinking of various investigators in the field, this book is extremely valuable.

The formally organized part of the book contains brief presentations of certain phases of the cerebrovascular problem, including pathology of cerebral vessels and lesions, hypertension, hemorrhage from aneurysms, estimation of cerebral blood flow, experimental cerebrovascular disease, experiments with enzymes, therapy of arteriosclerotic disease, anticoagulant therapy, and rehabilitation. A new system of classification and nomenclature is also presented.

Y. S.

► THE CERVICAL SYNDROME

By Ruth Jackson, M.D., Clinical Assistant Professor of Orthopedic Surgery, University of Texas Southwestern Medical School, Dallas. American Lecture Series. Ed. 2. 197 pages with 90 illustrations. 1958, Charles C Thomas, Springfield, Illinois. $6.50.

There are many features in the second edition of this timely and amazingly popular text that the first edition did not contain. Primarily, these additions emphasize the action of anatomic factors, particularly the vertebral artery and the dura mater, in producing cervical pain.

In regard to the mechanism and etiology of the cervical syndrome, the author has given more attention to the effects of dislocations, whether partial or complete, and to the causative role of inflammatory conditions and fractures in this troublesome entity. In the section on diagnosis, she has placed far more emphasis on the roentgenographic findings, particularly those from the lateral and oblique views, and has included numerous illustrations.

The second edition varies from the first also in that measures relating to treatment of the cervical syndrome have been expanded, and more case reports and examples from pertinent and informative cases have been included. In short, this expanded and augmented edition makes good some of the shortcomings of the original edition.

In almost all instances the illustrations serve the purpose for which they are intended. Drawings are used in proper places throughout the book to demonstrate ranges of motion and other maneuvers as well as the various devices for treatment. Excellent photographs of materials and methods of treatment are also included.

E. W. J.

► AUTOPSY
Diagnosis and Technic

By Otto Saphir, M.D., Pathologist, Michael Reese Hospital, Chicago. Ed. 4. 549 pages with 80 illustrations. 1958, Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York. $8.50.

The medical student who observes the performance of an autopsy, the assistant in the pathology laboratory, and the general practitioner who occasionally may be called on to perform an autopsy will find this very readable book a most useful guide. In addition to the description of a modification of Rokitansky's method, this new edition contains ample clear illustrations and several useful tables. The index is very completely prepared.

Three new chapters have been added, the first a short history of the autopsy written by Dr. Sidney Farber. The fifth chapter concerns autopsy on patients who have been exposed to or treated with radioisotopes. Precautionary measures in such cases are particularly important. The third new chapter is entitled "Tissue banking is becoming more common," and contains a discussion of autopsy tissue technics.

A. H. S.

(Continued on page A-162)

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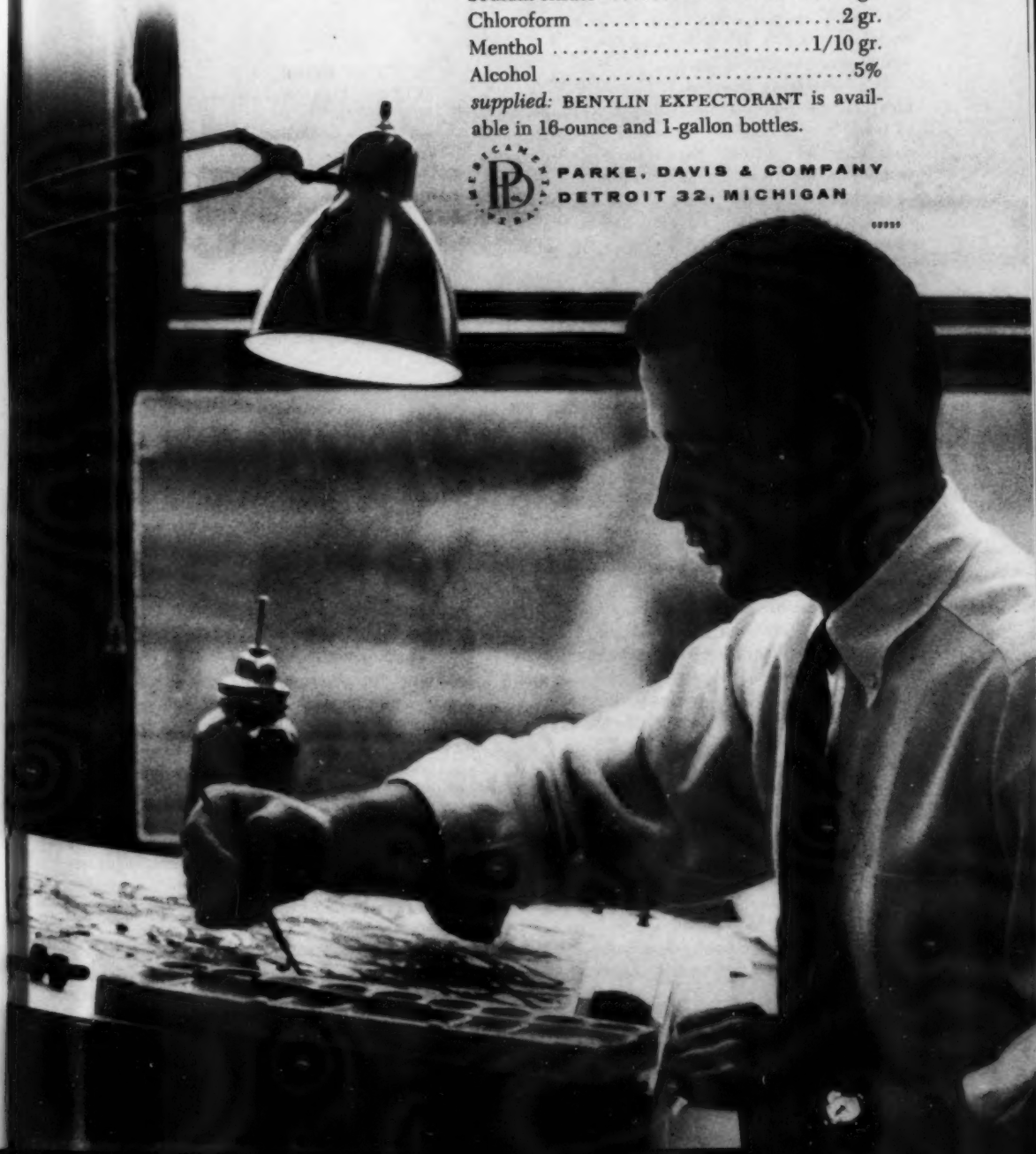

► TUMORS AND TUMOROUS CONDITIONS OF THE BONES AND JOINTS

By Henry L. Jaffe, M.D., Director of Laboratories and Pathologist, Hospital for Joint Diseases, New York. 629 pages with 701 illustrations. 1958, Lea & Febiger, Philadelphia. $18.50.

Through the years Dr. Jaffe has been a steady contributor to the literature on bone tumors, and his interest in this subject has led to his exceptional familiarity with the pathology of bone tumors and associated factors.

The material in this text is presented with the idea that the diagnosis and differential diagnosis of these tumors can best be accomplished if one considers the clinical, roentgenographic and pathologic features together. In the exposition of the various lesions, the author has relied on illustrative material to such an extent that the book could be considered an atlas of skeletal tumors. The author intended the book to be of assistance to pathologists, radiologists and orthopedic surgeons as well as to other medical personnel who are confronted by problems associated with the pathology of bone tumors.

In presenting the various pathologic problems, the author has followed the standard classifications, but he believes that these divisions are confining and that frequently it is valuable to consider each lesion as a separate clinicopathologic entity in its own right. Accordingly, he presents each entity as a separate condition, devoting adequate space to establishment of clear terminology, clinical consideration, roentgenologic and pathologic findings, differential diagnosis, and treatment. Elaborate use is made of the excellent illustrations which are well suited to the problem. Almost all the illustrations are accompanied by protocols bearing on the same problem, so that one can greatly increase his acquaintance with the clinical material by studying only the illustrations and their legends.

The chapter devoted to tumors developing at sites of pre-existing bone disease is particularly interesting and timely, as is a discussion of tumors complicating osteomyelitis and roentgen therapy. No attempt has been made to cover completely or list all the bibliographic material, but under each entity the author has used references liberally.

In large measure the book conveys the author's personal conceptions. Although they may vary somewhat from the reader's attitudes regarding certain clinical entities, such as giant-cell tumors, one must realize that Dr. Jaffe has some foundation for his judgments. Criticism of this fine volume would be directed to the categories related to treatment. However, it was not Dr. Jaffe's purpose to give a thorough discussion of treatment, and one should not expect a complete coverage of therapeutics in this excellent presentation of the pathology of bone tumors.

E. W. J.

► A TEXT-BOOK OF X-RAY DIAGNOSIS

Edited by S. Cochrane Shanks, M.D., Director, Diagnostic Department, University College Hospital, and Peter Kerley, M.D., Director, X-ray Department, Westminster Hospital, London, England, with 20 contributors. Ed. 3, vol. 3. 883 pages with 802 illustrations. 1958, W. B. Saunders Company, Philadelphia and London. $23.00.

The basic plan used in the first two editions of volume 2 of this work has been followed again in this edition. As might be anticipated, the headings of the different sections, ranging from the salivary glands through obstetrics, have been more or less retained, but the tremendous growth of radiology as a specialty is reflected in the text's actual bulk. The new additions are few when one compares this volume with its counterpart in the second edition, but they seem quite formidable when compared with the contents of the first edition. In addition, papers by several new contributors supplement and replace material from the long list of noted British radiologists.

Supplemental material has been added in sections dealing with the biliary tree and with the liver and visualization of its vascular bed. Some changes appear also in the urologic section. Although application of cineroentgenography is mentioned in relation to the study of motor physiology of the jejunum, it is not considered in studying deglutition, esophageal contractions or gastrointestinal diseases.

The illustrations are brilliant in quality. As in many non-American texts, the roentgenograms are negative rather than direct positive prints, with the exception of those used for the first time in this edition.

S. B. F.

(Continued on page A-164)

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► ILLUSTRATED PREOPERATIVE AND POSTOPERATIVE CARE

By Philip Thorek, M.D., Professor of Surgery, Cook County Graduate School of Medicine, Chicago. 98 pages with 60 illustrations. 1958, J. B. Lippincott Company, Philadelphia and Montreal. $5.00.

In the preface the author states that the material in this text was taken from his lecture notes and that he is attempting to present the fundamentals of preoperative and postoperative care without presenting the various theories related to this subject.

The first section, on preoperative care, is concerned with evaluation of the surgical candidate. The second and larger section, on postoperative care, contains chapters on the immediate postoperative period, the recovery room, use of parenterally administered fluids, acidosis and alkalosis, chemotherapy, ACTH, and complications of surgery, such as fever, bowel distention, urinary retention and others. There are also chapters on ambulation, use of morphine, and removal of sutures.

R. V. R.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers are reviewed more extensively.

Reversicon; a Medical Word Finder. By J. E. Schmidt, M.D., Chairman, National Association on Standard Medical Vocabulary. 440 pages. 1958, Charles C Thomas, Springfield, Illinois. $7.50.

Alcohol in Italian Culture. Monographs of the Yale Center of Alcohol Studies. By Giorgio Lolli, M.D., Formerly, Director, Yale Plan Clinic, Emidio Serianni, M.D., Director, Instituto di Alimentazione e Dietologia, Rome, Italy, Grace M. Golder, M.S., Formerly, Research Assistant, Yale Plan Clinic, New Haven, and Pierpaolo Luzzatto-Fegiz, LL.D., Professor of Statistics, University of Trieste, Trieste, Italy. No. 3. 140 pages. 1958, Publications Division, Yale Center of Alcohol Studies, New Haven, and The Free Press, Glencoe, Illinois. $4.00.

Manual of Blood Morphology. By Lydia Schudel, University of Zurich, Zurich, Switzerland. Ed. 9. 54 pages with 18 color tables. 1958, Georg Thieme Verlag, Stuttgart, Germany. Distributed in the United States and Canada by Intercontinental Medical Book Corporation, New York. $3.50.

Essentials of Therapeutic Nutrition. By Solomon Garb, M.D., Associate Professor of Pharmacology, Albany Medical College, Albany. 147 pages. 1958, Springer Publishing Company, Inc., New York. $2.00.

Self-Destruction. A study of the suicidal impulse. By Beulah Chamberlain Bosselman, M.D., Professor of Psychiatry, University of Illinois College of Medicine, Chicago. 94 pages. 1958, Charles C Thomas, Springfield, Illinois. $4.75.

Cyclopropane Anesthesia. By Benjamin Howard Robbins, M.D., Professor of Anesthesiology, Vanderbilt University School of Medicine, Nashville. Ed. 2. 293 pages with 74 illustrations. 1958, The Williams & Wilkins Company, Baltimore. $9.00.

Annals of The New York Academy of Sciences, 1958: Genetic Concept for the Origin of Cancer. Vol. 71, Art. 6. 435 pages, illustrated, $5.00. Lymphocytes and Plasmacytes in Nucleoprotein Metabolism. Vol. 72, Art. 9. 46 pages, $2.00. Hodgkin's Disease. Vol. 73, Art. 1. 380 pages, illustrated, $4.50. Surgical Convalescence. Vol. 73, Art. 2. 158 pages, illustrated, $4.00. Third Tissue Homotransplantation Conference. Vol. 73, Art. 3. 230 pages, illustrated, $5.00. Contributions of the Physical, Biological and Psychological Sciences in Human Disability. Vol. 74, Art. 1. 160 pages, illustrated, $3.50. Enzymes in Blood. Vol. 75, Art. 1. 384 pages, illustrated, $5.00. The Basic and Clinical Research of the New Antibiotic Kanamycin. Vol. 76, Art. 2. 392 pages, illustrated. $5.00.

Medulloblastoma. American Lecture Series. By Benjamin L. Crue, Jr., M.D., Neurosurgical Service, U. S. Naval Hospital, San Diego. 206 pages, illustrated. 1958, Charles C Thomas, Springfield, Illinois. $5.75.

Antibiotics Monographs. Chloromycetin (Chloramphenicol). By Theodore E. Woodward, M.D. and Charles L. Wisseman, Jr., M.D., Baltimore. No. 8. 159 pages, $4.00. Penicillin. By Harold L. Hirsch, M.D. and Lawrence E. Putnam, M.D., Washington, D.C. No. 9. 148 pages, $4.00. Streptomycin and Dihydrostreptomycin. By Louis Weinstein, M.D., Boston, and N. Joel Ehrenkranz, M.D., Miami. No. 10. 116 pages with 13 illustrations, $4.00. Modern Chemotherapy of Tuberculosis. By Roger S. Mitchell, M.D. and J. Carroll Bell, M.D., Denver. No. 11. 109 pages, $4.00. 1958, Medical Encyclopedia, Inc., New York.

Food and You. By Edmund Sigurd Nasset, Ph.D., Professor of Physiology, University of Rochester School of Medicine and Dentistry, Rochester, New York. Ed. 2. 166 pages. 1958, Barnes & Noble, Inc., New York. $1.25.

The Birth of Normal Babies. By Lyon P. Strean, Ph.D., Consultant, Norristown State and Montgomery Hospitals, Norristown, Pennsylvania. 194 pages. 1958, Twayne Publishers, Inc., New York. $3.95.

The World Traveler's Medical Guide. By Richard Travis Atkins, M.D. and Jane McGlennon Atkins, B.S., Old Greenwich, Connecticut. 399 pages. 1958, Simon and Schuster, Inc., New York. $1.95.

Sensitivity Reactions to Drugs. A symposium organized by The Council for International Organizations of Medical Sciences. Edited by M. L. Rosenheim and R. Moulton, University College Hospital Medical School, London, England. 237 pages, illustrated. 1958, Charles C Thomas, Springfield, Illinois. $7.00.

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DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Dec. 1—To the North Shore for luncheon with the Big Sisters, riding with Persis Sachs and Mrs. Frank and discoursing on philanthropic activities. So heard the reports of the officers and a tale of rehabilitation of a disconsola.e damsel. Then spoke to them concerning the difficulties of knowing what was scientific in the field of psychology.

Dec. 2—By the morning plane to Boston and to the University Club for luncheon with Charles Haney. Next to drive to Everett for an interview on radio with Dr. James R. Corkery, who did well for his first performance. At night to the armory for a dinner with some 900 people. Here spoke Drs. Charles Wilinsky and Corkery; met Miss Evelyn Morgan and Dr. Olga Leary, the pathologist, and altogether an enjoyable occasion with many friends.

Dec. 3—To the Retina Foundation to discuss developments, meeting with Denholm Jacobs and Drs. Charles L. Schepens and Endre A. Balazs and Miss Lilian M. Clancy, who graciously praised "Medical Writing." Next comes Bill Haney, and with him to view the suburb of Chelsea, which is in need of renewal, and its hospital, which faces a crisis and is in even greater need. In the afternoon defeated in mathematics by Charles Wilinsky, who had great joy in his victory. Then to a cocktail party, meeting most of the medicos, many Phi Delta Epsilons, in particular the H. Arthur Bersons and Jacob Burkes, and sat with Mrs. Annabelle Berson, who is chief of the Aid. At the dinner were some 600 of the citizenry, and fine speeches were made by Drs. William P. Finnegan, Nicholas Gianturco and Hagopian, with much scurrying back and forth for obstetrics in progress.

Dec. 4—Back by plane and in the evening to hear Fritz Reiner and the beauteous soprano Lisa Della Casa. Then to be interviewed by Tony Weitzel on radio, along with the movie stars Inger Stevens and Russ Tamblyn, two intense and more than intelligent young people, she being interested in the handicapped and he in writing.

Dec. 5—To luncheon with Sam Baskin and Dachman at the Covenant Club and planned for the great dinner to come on Sunday, December 6. The whole apartment bedecked with flowers and much running hither and thither of helpers. In the afternoon came Basil and Hazel O'Connor and to pay courtesy to them some hundreds of our friends, including Ben Willis, superintendent of our schools, Howard Willett, Judges Brown and Braude, Carol Fox and Howard Larkin, Flanagan, Sheinin, LeRoy, Karl Meyer, Dan Ryan, the Kirsners, the Davises and Lewin. At night to the Empire Room, where Fritz outdid even his best in the service and the Chavales performed excellently. Here saw Dean Lierle of Iowa, and arranged to give a course on writing to the triological when next it meets.

Dec. 7—In the afternoon came the physical therapists and the overflow of guests, and then all to the Hilton, where some 600 assembled in a "Salute to Medical Research," sponsored by the City of Hope and the Illinois Society for Medical Research. Pierre De Mets had planned perfectly. Bishop Ezekiel and Rabbi Louis Mann gave prayers, Sam Baskin "toastmastered" felicitously, George LeRoy gave a citation to Charles Huggins, Pres. Elvehjem of the University of Wisconsin did the same for Szent-Györgyi, and President David Henry of the University of Illinois for Basil O'Connor. The talks were informal and delightful. Then Paul Wermer spoke for the City of Hope and presented an unexpected citation to old Pepys who was most happy. On the dais were Mages, Ratner, Ross Harrison, Longenecker, Brewer, Klapman, De Mets, Francois Pope and all the medical officialdom. Old Pepys spoke of chauvinism in research. The Liefermans and Schneiders presented awards to Huggins and Szent-Györgyi for their research, and Basil O'Connor spoke of the great need for private initiative and philanthropy in achieving great objectives.

(Continued on page A-192)

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1. Menger, H. C.: J.A.M.A. 159:546 (Oct. 8) 1955.
2. Published and unpublished case reports.

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3764

Dec. 8—In the morning with Lippincott's Walter Kahoe, discussing medical affairs and "Medical Science." In the afternoon planning with Paul Wermer the new Institute for Advanced Learning in the Medical Sciences. In between, reading "The Madhouse in Washington Square," by David Alexander, which is not worth even the little time it took, and "The Dead Man's Knock," by John Dickson Carr, who writes superbly, but this book is a little "odd ball," too.

Dec. 9—At noon to the Rotary Club and heard two young men tell how much a fellowship had done for them. Thereafter to the American Academy of Dermatology, viewing the exhibits and chatting with Cornbleet, Jacobs, Beinhauer of Pittsburgh, and Mark Soroko. In the evening to dine at Andy's Epicurean on chicken paprika and sherry, cheese and apple strudel, and had fine conversation with Ted Sternberg of Los Angeles and his lovely lady about Norm Topping and the topic of education in southern California.

Dec. 10—To the Cook County Hospital to speak after Fred Hertwig and Karl Meyer about the history of surgical sterilization. For lunch came Herman Fussler, librarian at the University of Chicago, about a newly offered collection of old medical writings. Reading now "Mistress to an Age," by Christopher Herold, which is a beautifully written life of Madame de Staël, and amazed to know of her mother's relationship to Edward Gibbon, William Pitt and, particularly, to her father, the great Necker.

Dec. 11—All the day at the desk and in the evening to hear again our orchestra and Casadesus in a well-nigh perfect rendering of Saint-Saëns.

Dec. 12—At noon to meet with the University of Chicago Cancer Research Foundation, where Maurice Goldblatt presided; talks were made by Lowell Coggeshall, M. Edward Davis and Vice-chancellor Kirkpatrick. Funds rise apace, and a new diagnostic center is contemplated. Old Pepys presented a contribution from the Cancer Research Foundation. In the evening to Judge Brown's for dinner with Judges Gutknecht, Marovitz and Burke, and Sensibars and Mockleys, and all the talk was of Russia—of how far she has advanced and the seriousness of her threats.

Dec. 13—Lester Marks is now hospitalized with what the medicos call a slight coronary. The cold is below zero and the snow mantles the earth. So sat at home reading of Madame de Staël—what a dame! But she couldn't fool Napoleon. Watched the Cardinals defeat Pittsburgh and also saw a good basketball game.

Dec. 14—Early to Highland Park to visit the children and grandchildren and spent some time with Drs. Max Schneider and Morris Friedell, viewing electrocardiograms and laboratory reports.

Dec. 15—Preparing copy for "Medical Science," *McCall's*, *World-Wide Abstracts* and POSTGRADUATE MEDICINE. What fun! In the afternoon with Mistress Pepys to mail Christmas packages. At night to see again Peter Ustinov in "Romanoff and Juliet," with a first-night audience that laughed till the tears came and gave an ovation at the end. But, unfortunately, some supporting actors did not equal the London cast.

Dec. 16—At the desk, still reading the amazing history of Madame de Staël, and especially interested in her visits to writers Goethe and Schiller and her affair with Von Schlegel. At noon to a luncheon with A. Sachar of Brandeis and heard they will soon have a two year basic science medical school, and their department of biochemistry is already one of the best. In the evening to the new Chippendale Room in the Ambassador West to dine as guests of Mr. and Mrs. Pat Hoy for the annual meeting of the Municipal Tuberculosis Sanitarium. Mayor Daley graced the occasion; Ernest Irons reported; and Drs. Lichtenstein, Tamar, Bundesen, Karl Meyer and all the staff contributed observations. Thereafter to the Feiwells', who entertained for the Schuhmanns, and exchanged witticisms with Falstein anent medical humor. He told of a gynecologist to whom a patient came at the end of the office hours. He told her his nurse already had gone and the hour was too late for an examination, so they gossiped and shared some Martinis. Suddenly, he observed that his wife's car was stopping at the curb. "Get undressed quickly," he said to the patient, "my wife's coming."

(Continued on page A-194)

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Supplied: MODERIL Tablets—yellow, scored 0.25 mg. oval tablets, bottles of 100 and 500; salmon, scored 0.5 mg. oval tablets, bottles of 100.

Dosage: The recommended initial dosage is 0.5 mg. twice daily for two weeks, with reduction thereafter to a minimum maintenance dosage of 0.25 mg. once daily. For greater hypotensive effect after initial period, increase dosage cautiously by 0.25 mg. daily up to a maximum daily dosage of 2.0 mg. Prescribe after meals.

1 Moyer, J. H., et al.: A.M.A. Arch. Int. Med. 96:530, 1955. 2. Moyer, J. H., et al.: South. M. J. 50:499, 1957. 3. Smirk, F. H., and McQueen, E. G.: Lancet 2:115, 1955. 4. Winton, S. S.: Internat. Rec. Med. 170:665, 1957. 5 Malamud, W., et al.: Am. J Psychiat 114:193, 1957.

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Dec. 17—Finished "Mistress to an Age," and what a woman was this Madame de Staël and how weird her relationships with Benjamin Constant, Von Schlegel, Rocca, Napoleon, Madame Récamier, Lord Byron and also Goethe! What a life it was, with dependence on opium and sex for its stimulation to literature! At noon to luncheon with Irving Harris and the psychologist Neuman, discussing means of finding an aptitude toward creativity. Then reading the special issue of the *Scientific American* on the same subject. At night to dine in the Beau Nash Room of the Ambassador with the Joselits, Sterns, Grawoigs, Frieders and Schuhmanns—good food and good fun.

Dec. 18—At noon to the board meeting of the Lyric Opera at the University Club, completing plans for 1959 and 1960. Then to mail a dozen packages, finding a long line of Christmas package mailers. In the evening a buffet at the Shoreland and played bingo, once coming within one number.

Dec. 19—At noon luncheon with Holland, Dachman and Weinstein, planning next year's "Salute to Medical Research." In the afternoon entertained Ed Schuhmann by a small contribution in gin—the lucky stiff! In the evening arrived four little grandchildren for a week-end visit, so serious activities were adjourned.

Dec. 20—To the Variety Club, where the barkers entertained some 50 small fry with a luncheon, a magician and gifts, Bill Margolis presiding. And all the small fry told the magician they knew how his tricks were done. Then to the Standard Club for some more entertainment, and

THE OLD ONES ARE THE BEST

The sick were lined up for a block outside a clinic in the Bronx. One fat little man seemed especially eager to get in. Calmly he walked to the head of the line. Thirty people yelled their protests and squeezed him out. The little man got up, dusted himself off and tried again, again to be ejected. One big man grabbed him and growled: "Listen! You wait your turn like the rest of us!"

"You listen! Throw me out of line once more, and I won't open the clinic!" protested the doctor.

* * *

about 200 small fry were delighted with the puppets and canine performers.

Dec. 21—To the Tavern Club, with the small fry watching cartoon movies, magicians and trained dogs with a monkey, and Santa Claus came bearing gifts. Well, that's Christmas! Reading now Marquand's "Women and Thomas Harrow," exemplifying the wonderful skill in style and diction typical of Marquand.

Dec. 22—At noon to the Prudential building for lunch with Bob Hardt, new president of Armour Laboratories, talking about new research. Thereafter in the shops and bookstores and back to the desk.

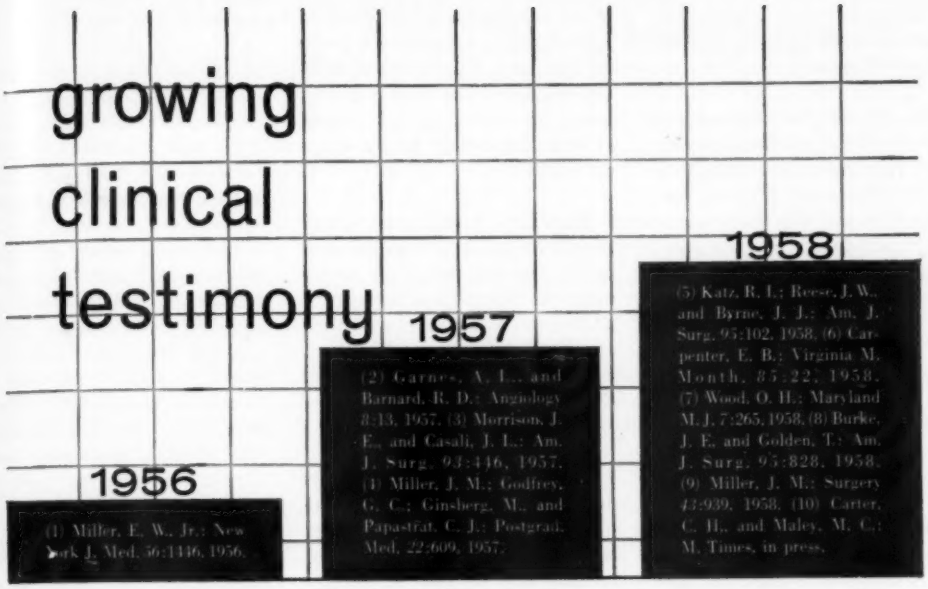
Dec. 23—To the Crerar Library, where Ella Salmonsen prepared for me the first issue of all the periodicals in cardiology. Then to Rotary, sitting with Sidney Wanzer, who provided eggnog for all the tables, and Gene Stein and Stanley Clague of *Modern Hospital*. So heard the singing, and the gifts were distributed; also saw Egdorf, Murray Kornfeld and many others.

Dec. 24—At the desk while Mistress Pepys is wrapping, packing and labeling. In the afternoon to the Pump Room, being interviewed on radio by Bob Elson for a half-hour. Next to the Standard Club, meeting dozens of friends, all high in praise of "Dr. Pepys' Pages," but too many to mention. Then to the Tavern Club for more of the same, chatting with Paul Angle, the historian, and Emmett Dedmon, the editor, and saw Judge Julius Hoffman and Dr. Harry Hoffman dining with their ladies while old Pepys did the same with the children and in-laws.

Dec. 25—Early awake and after opening many packages to see Charles Lawrence, who was still waking up, although the little girls were wide-eyed. Then to La Rabida, where 100 little ones with rheumatic fever were cheered by Santa Claus. For one little girl, aged 12, it was her sixth Christmas in the hospital. Here were the Frieders bearing gifts, Helen Kahn, Pierre De Mets, and Al Dorfman, and for all the ladies an emotion-filled morning. Next to Marjorie Marks' for lunch with the children and after that to Highland Park Hospital to see Lester well on the road to recovery. After that to Barbara's, where Justin came with all the children and also Sam Hoffman, and the day finished happily.

Dec. 26—At noon came Nick and Andy Dontas and the latter's lady, who is also a doctor, and they told us news of Bailey in Philadelphia and of Ancel Keys in Minneapolis. In the afternoon to the Museum of Science to see exhibits. Then for cocktails with Edmund Jacobson, who was relaxed, and then to the Friedells' for dinner. So drove home with Buddy Haas, who has a telephone in his car and says it pays if he makes only one call a year. In

(Continued on page A-196)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- **Papain**, the proteolytic enzyme—digests necrotic tissue and liquefies exudate without harm to healthy tissue—eliminates local infection by removing the bacteria-supporting substrate.
- **Urea**, the protein-solvent—augments the debriding action of papain by exposing protein substrates to complete proteolysis.
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PACKAGING: Available *on prescription only* in 1-oz. and 4-oz. tubes.

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the night finished "Women and Thomas Harrow," which is charming, contemplative and full of fun and satire.

Dec. 27—To the Drake to talk at the luncheon of Phi Delta Epsilon. Then played gin with Monroe Greenberger, Brooks and Fink; at night was toastmaster, being introduced by Aaronson, the allergist; prizes were awarded by A. Rechtman of Philadelphia and by Greenberger. Emil Rothman, Detroit, outgoing president, spoke, as did Harold Brandeleone, incoming chief. Then B. Edgar Spiegel presented Dr. Sidney Farber, who received the grand award of the fraternity.

Dec. 28—To a brunch in five national cookeries at the Drake—wholly delightful—and congratulated Dick Flynn on the arrangements. So sat with the Pilots, Pearlmans and Weisses, and then watched the Baltimore Colts win a thrilling game by a touchdown in the sudden-death overtime. At night reading a half-dozen medical journals, finding some striking articles in the *Annals of Surgery*, the *New England Journal of Medicine* and the *British Medical Journal*.

Dec. 29—At the desk writing thank-you notes. In the afternoon to the Heart Association to discuss with Grimes and Roberg the problem of ambulances and heart attacks. Later to talk with Albert and Justin, and reflected on the death of Joe Fay, which saddened all the newspaper profession.

Dec. 30—All this day at the desk and reading now "The Visitors," by Mary McMinnies, which is a gorgeous fiction of an Englishman and his wife on foreign service in a country that might well have been Poland. The novel is a satiric view of life under communism, with remarkable insight into a nation governed with a view to propaganda.

Dec. 31—At noon to visit the painter John Doctoroff in his studio. In contemplation of the year that is ending, old Pepys believes that the world does not seem so much different from what it was at the end of 1957. The politicians—medical and governmental—still seek to sway their followings, and the result is instability and doubt. The stock market continues to rise but seems to totter with even more instability at its heights. The athletes alone continue to produce new peaks of excitement and interest and even at their peak show the inevitable failings that come with human emotions. And television, inundated with Westerns, crime and miserable rock-and-roll music, seems to have gone further and further backward with time in its flight. Fortunately there is still Jack Paar.

The Medical Muse

RICHARD ARMOUR

NOTE FOR OBSTETRICIANS

There is a term to which, my friends,
I heartily object,
A word that, in the way it's used,
Is simply not correct.

"Delivery" is what I mean,
A term that has a mission
With milkman, postman, many more,
But not the obstetrician.

Here's what has puzzled me for years,
Though no one seems to care:
How can a person possibly
Bring what's already there?

STAYING PUT

The doctor notes with satisfaction
His patient trussed and tied in traction.
A job well done, it is, and tight,
And everything bound up just right.

But though my statement may seem snide,
I'll have to say it isn't pride,
Or pride alone, that gives this feeling
And makes the scene so darned appealing.

There's also this: now for a little,
The patient, who is rather brittle,
Won't fall down steps, won't stub on rubble,
And you can find him without trouble.